THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Optimizing exercise prehabilitation in cancer care

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Energy Balance Research Seminar
June 4th, 2020
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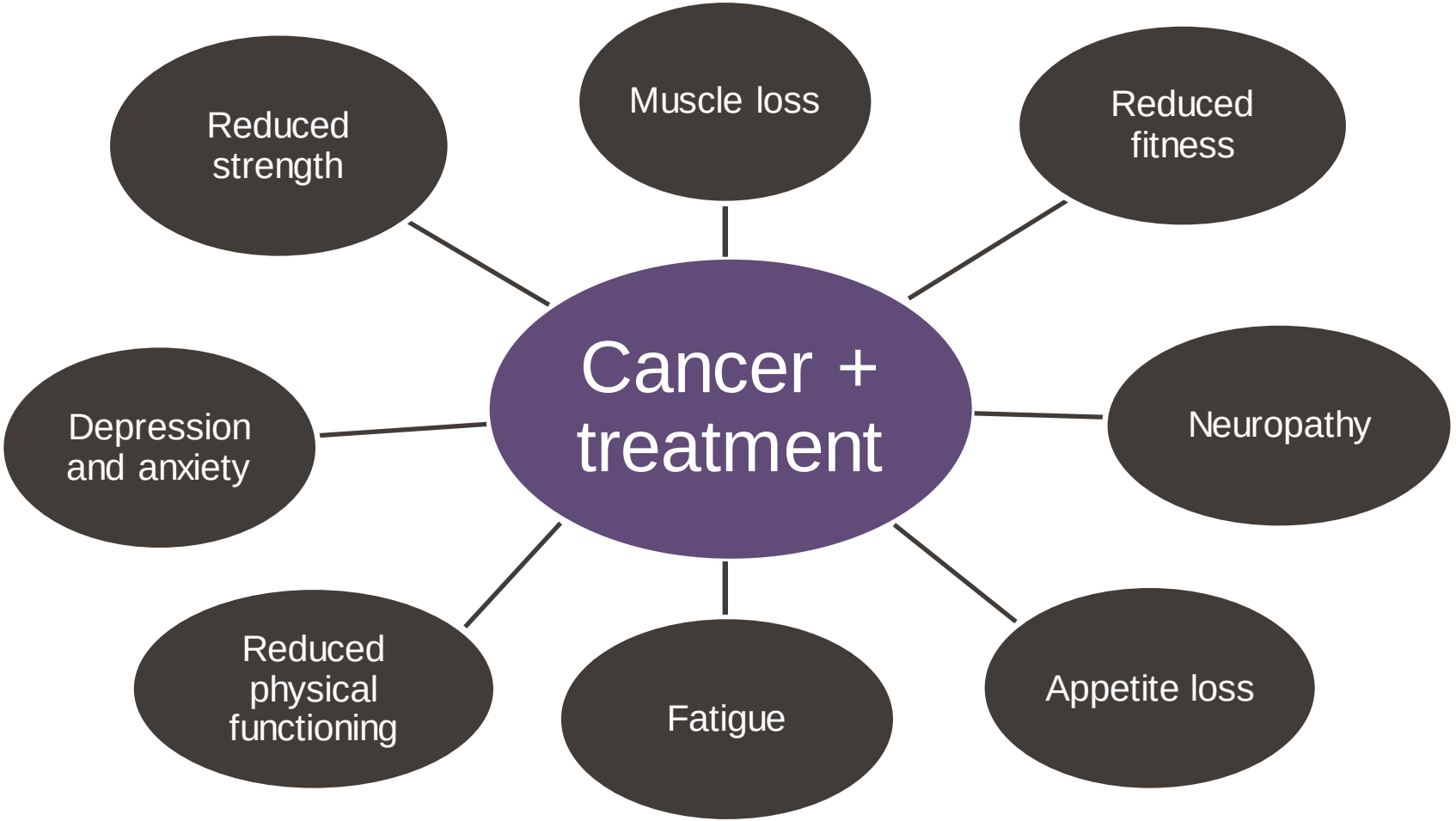
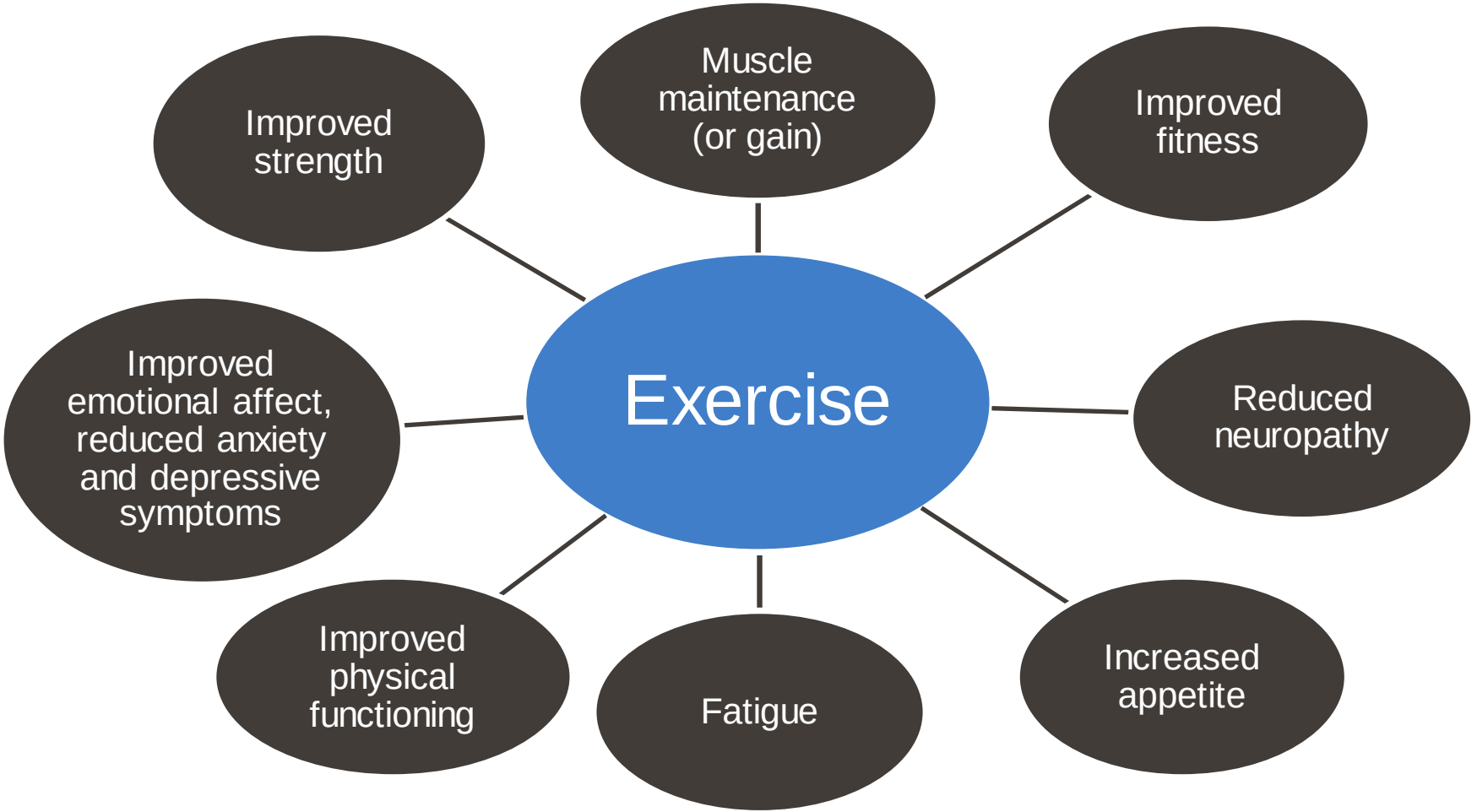
Objectives

- Describe the rationale for exercise prehabilitation in cancer care
- Provide an overview of findings from previous cancer prehabilitation studies
- Provide an overview of pancreatic cancer prehabilitation at MD Anderson
- Describe current and next steps in exercise prehabilitation for cancer


Cancer + treatment
Reduced strength
Muscle loss
Reduced fitness
Depression and anxiety
Neuropathy
Reduced physical functioning
Fatigue
Appetite loss


Exercise
Improved strength
Muscle maintenance (or gain)
Improved fitness
Improved emotional affect, reduced anxiety and depressive symptoms
Reduced neuropathy
Improved physical functioning
Fatigue
Increased appetite

American College of Sports Medicine Exercise Guidelines for Cancer Survivors (2019 updates)

- Updated evidence for dose-response relationships between exercise and outcomes in cancer survivorship.

≥30 minutes moderate-intensity aerobic exercise ≥3x/week

AND

≥2 weekly sessions of resistance training targeting major muscle groups (≥2 sets of 8-15 repetitions at ≥60% of 1-repetition maximum)

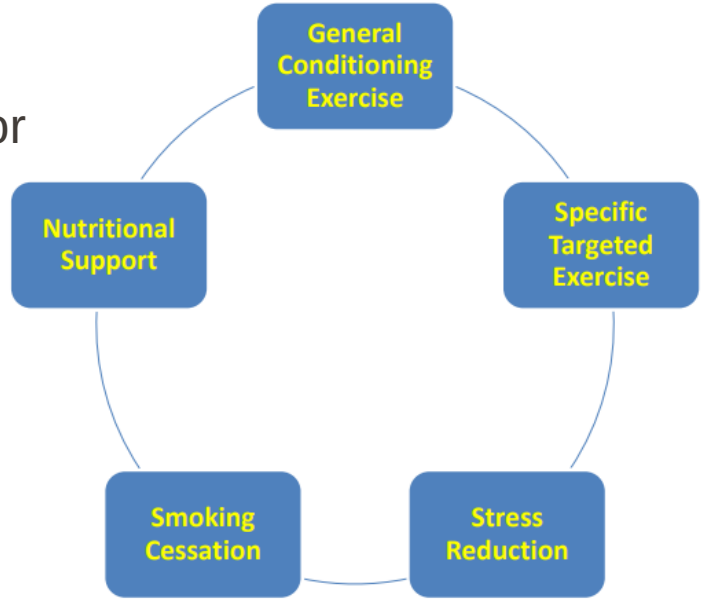
- **Adapt** according to age, treatment, limitations, performance status

Campbell et al., 2019

AMERICAN COLLEGE of SPORTS MEDICINE
LEADING THE WAY

Cancer prehabilitation

- Goals
  - Optimize health before cancer treatments
  - Prevent impairments and reduce the need for reconditioning
- Targets
  - Surgical and perioperative outcomes
  - Physical functioning
  - Fitness
  - Body composition
  - Psychological well-being
  - Health-related quality of life

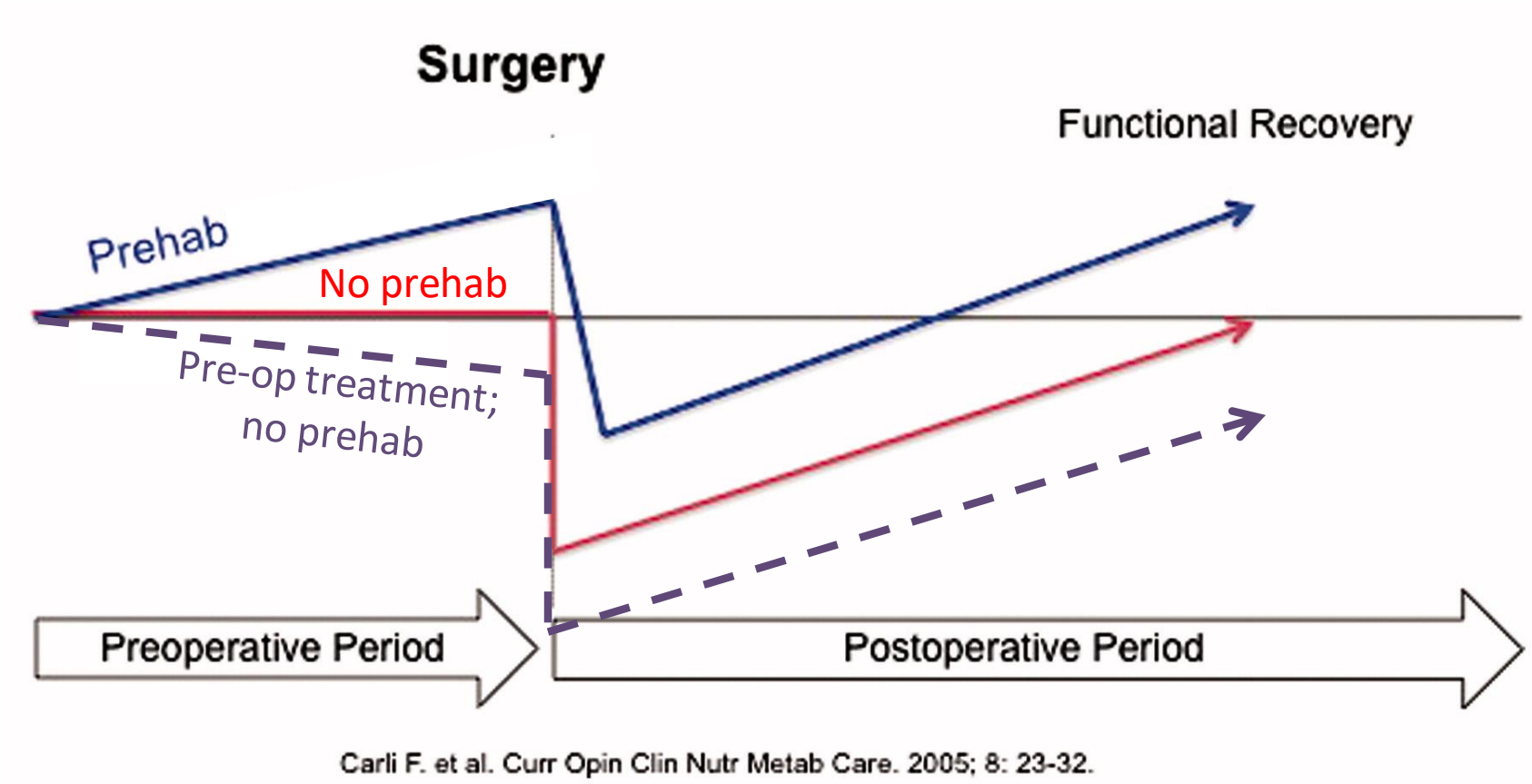


Silver JK, Baima J, Mayer RS. Impairment-driven cancer rehabilitation: an essential component of quality care and survivorship. *CA Cancer J Clin.* 2013;63(5):295-317.

TABLE 3 Goals and benefits of cancer prehabilitation[a]

Pretreatment baseline	Assess and document
Pretreatment impairments	Identify and reduce
Pretreatment physical functioning	Improve
Pretreatment psychological functioning	Improve
Treatment options	Increase
Cancer treatment compliance	Increase
Treatment-related impairments	Prevent or reduce
Unnecessary testing[b]	Reduce
Time to recovery milestones	Reduce
Hospital lengths of stay	Reduce
Home care therapy visits	Reduce
Rehabilitation outpatient visits	Reduce
Hospital readmissions	Reduce
Risk for future comorbidities[c]	Reduce
Risk for cancer recurrence	Reduce
Risk for second primary cancer	Reduce
Disability	Decrease
Mortality	Decrease
Physical health outcomes	Improve
Psychosocial health outcomes	Improve
Time to return to work status	Reduce
Occupational function	Improve
Health-related quality-of-life	Improve
Direct healthcare costs	Decrease
Indirect healthcare costs	Decrease

Silver and Baima, Am J Phys Med Rehabil (2013)



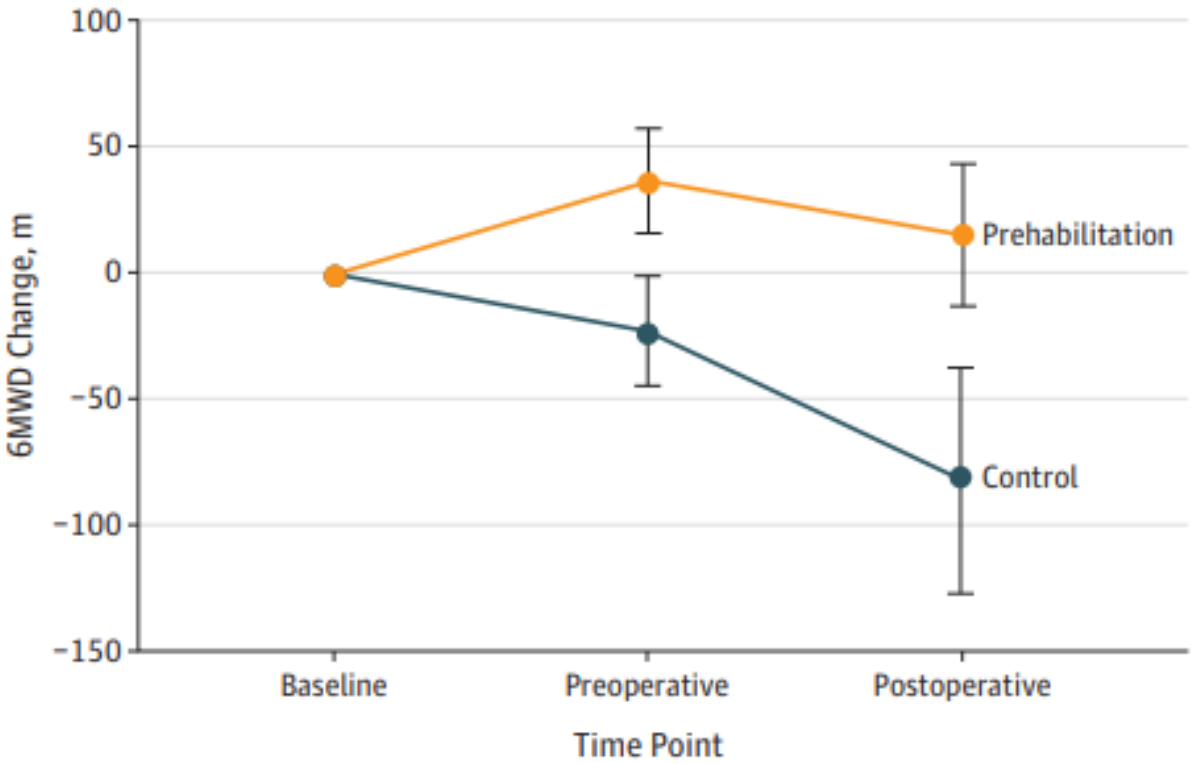
Carli F. et al. Curr Opin Clin Nutr Metab Care. 2005; 8: 23-32.

Esophogastric cancer

Prehab (5 weeks) and perioperative **6-minute walk distance** for surgery patients

Prehab *n*=26
Control *n*=25

*significantly better improvement in aerobic functioning in the prehab group (*p*<.001)



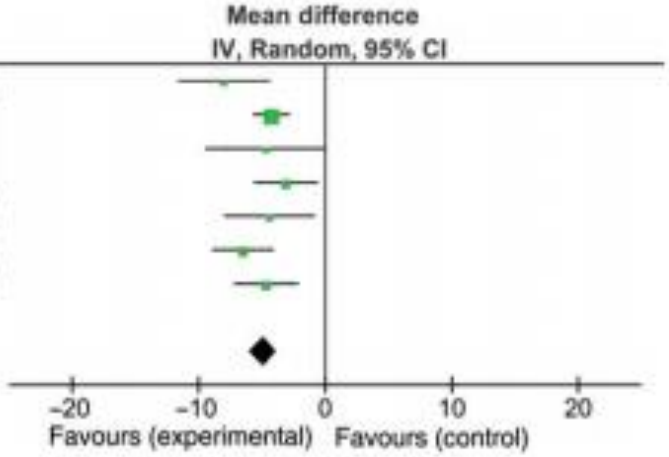
Minnella et al., *JAMA Surgery* (2018)

Lung cancer

Study or subgroup	Rehabilitation Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI	Year
Sekine et al., 2005	21	6.8	22	29	9	60	7.9%	−8.00 [−11.64, −4.36]	2005
Pehlivan et al., 2011	5.4	2.67	30	9.66	3.09	30	33.8%	−4.26 [−5.72, −2.80]	2011
Benzo et al., 2011	6.3	3	9	11	6.3	8	4.8%	−4.70 [−9.49, 0.09]	2011
Fang et al., 2013	11.8	3.23	22	14.9	5.16	22	14.9%	−3.10 [−5.64, −0.56]	2013
Morano et al., 2013	7.8	4.8	12	12.2	3.6	9	8.1%	−4.40 [−7.99, −0.81]	2013
Bradley et al., 2013	9.25	6.53	58	15.75	15.97	305	15.7%	−6.50 [−8.96, −4.04]	2013
Gao et al., 2014	14.54	4.71	71	19.21	9.89	71	14.8%	−4.67 [−7.22, −2.12]	2014
Total (95% CI)			224			505	100.0%	−4.83 [−5.90, -3.76]	

Heterogeneity: $\tau^2 = 0.33$; $\chi^2 = 7.10$, df = 6 ($P = 0.31$); $I^2 = 15\%$

Test for overall effect: $Z = 8.83$ ($P < 0.00001$)



Meta-analysis and pooled estimated effect size for **postoperative length of stay** in prehab intervention group and control group

Significantly reduced postoperative length of stay (~5 days difference) in prehab patients vs. control patients following surgical resection of lung cancer.

Attitudes and Perceptions to Prehabilitation in Lung Cancer

Integrative Cancer Therapies
Volume 19: 1–6

Anna Shukla, BAppSc[1,2], Catherine L. Granger, B Physio(Hons), PhD[1,3], Gavin M. Wright, MBBS, FRACS, PhD[2,4], Lara Edbrooke, BAppSc, PhD[1,5], and Linda Denehy, BAppSc, PhD[1,5]

Abstract

Background: Prehabilitation to maximize exercise capacity before lung cancer surgery has the potential to improve operative tolerability and patient outcomes. However, translation of this evidence into clinical practice is limited. **Aims:** To determine the acceptability and perceived benefit of prehabilitation in lung cancer among thoracic surgeons. **Procedure:** 198 cardiothoracic surgeons within Australia and New Zealand were surveyed to evaluate their attitudes and perceived benefits of prehabilitation in lung cancer. **Results:** Response rate was 14%. A moderate proportion of respondents reported that there is a need to refer lung resection patients to preoperative physiotherapy/prehabilitation, particularly high-risk patients or those with borderline fitness for surgery. 91% of surgeons were willing to delay surgery (as indicated by cancer stage/type) to optimize patients via prehabilitation. The main barriers to prehabilitation reported were patient comorbidities and access to allied health professionals, with 33% stating that they were unsure who to refer to for prehabilitation in thoracic surgery. This is despite 60% of the cohort reporting that pulmonary rehabilitation is available as a preoperative resource. 92% of respondents believe that further research into prehabilitation in lung cancer is warranted. **Conclusion:** The benefits of prehabilitation for the oncology population have been well documented in the literature over recent years and this is reflected in the perceptions surgeons had on the benefits of prehabilitation for their patients. This survey demonstrates an interest among cardiothoracic surgeons in favor of prehabilitation, and therefore further research and demonstration of its benefit is needed in lung cancer to facilitate implementation into practice.

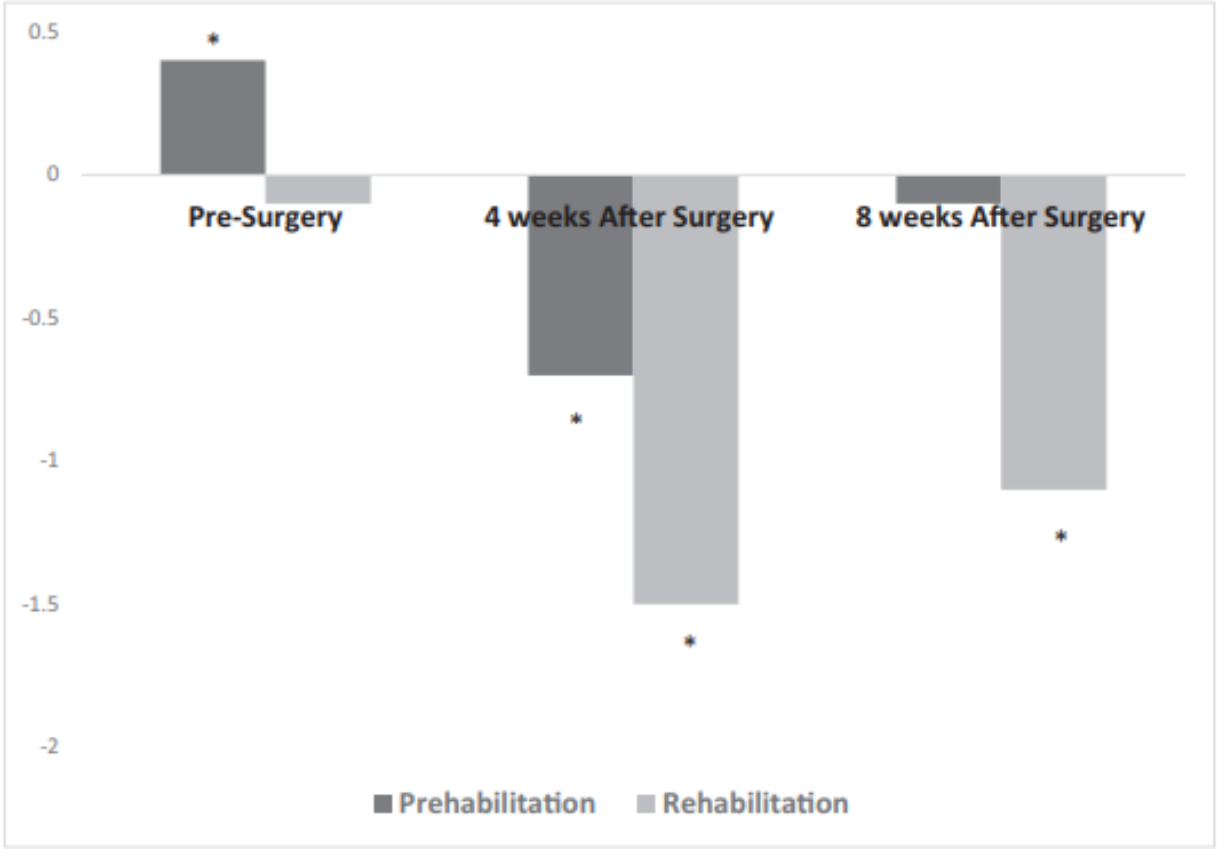
Colorectal cancer

Pooled analysis of interventions for surgery patients

Unadjusted mean changes in absolute lean mass

Prehab *n*=76
Rehab *n*=63

*statistically significant change relative to baseline ($p<.05$)



Gillis et al., *Clinical Nutrition* (2018)

…but there are some mixed findings

Gastroenterology > Colon Cancer

Can 'Prehabilitation' Help Frail Colorectal Cancer Patients Undergoing Surgery?

— First randomized trial of multi-part behavioral program

MEDPAGE TODAY®

by Diana Swift, Contributing Writer January 23, 2020

Multimodal "prehabilitation" did not improve 30-day postoperative outcomes versus postoperative rehabilitation in frail elderly patients undergoing colorectal cancer resection, a randomized trial found.

The two-site study by Francesco Carli, MD, MPhil, of McGill University Health Centre in Montreal, and colleagues found no inter-group difference in the primary outcome measure, the 30-day Comprehensive Complications Index, for an adjusted mean difference of −3.2 (95% CI −11.8 to 5.3, *P*=0.45). Nor was there a difference in secondary postoperative measures, including 30-day overall and severe complications, primary and total length of hospital stay, 30-day emergency department visits and readmissions, recovery of walking capacity, or patient-reported outcomes.

JAMA Surgery | Original Investigation

Effect of Multimodal Prehabilitation vs Postoperative Rehabilitation on 30-Day Postoperative Complications for Frail Patients Undergoing Resection of Colorectal Cancer

A Randomized Clinical Trial

JAMA Surgery March 2020 Volume 155, Number 3

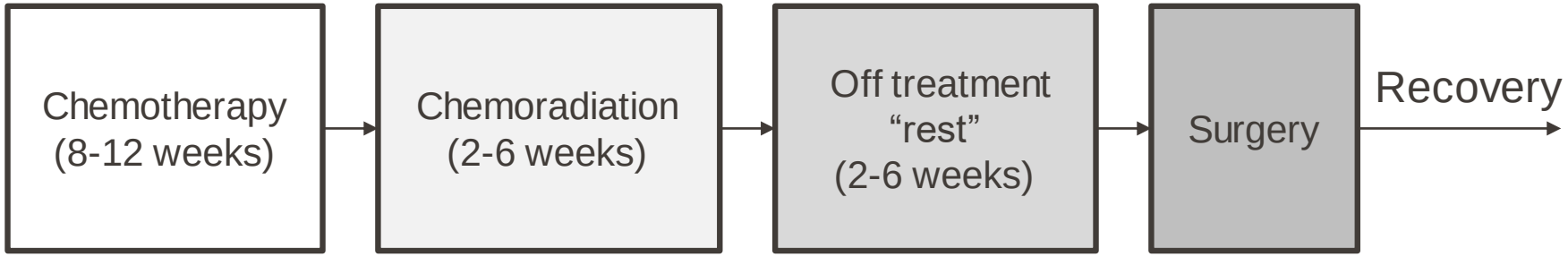
Francesco Carli, MD, MPhil; Guillaume Bousquet-Dion, MD; Rashami Awasthi, MSc; Noha Elsherbini; Sender Liberman, MD; Marylise Boutros, MD; Barry Stein, MD; Patrick Charlebois, MD; Gabriela Ghitulescu, MD; Nancy Morin, MD; Thomas Jagoe, MD; Celena Scheede-Bergdahl, PhD; Enrico Maria Minnella, MD, PhD; Julio F. Fiore Jr, PhD

- Two centers with well-established enhanced recovery pathways and ~80% of patients underwent minimally invasive surgery
  - "Effects of prehabilitation may be limited when other aspects of perioperative care are already optimized."
- Prehabilitation program was 4-5 weeks
  - Significant increases in lean body mass, muscular strength, and functional capacity require at least 12 weeks in elderly patients, even with intense exercise and protein supplementation (Karelis et al., 2015)
  - Short programs may provide insufficient anabolic stimulus and fail to "move the needle" on surgery-related outcomes

Exercise prehabilitation during preoperative treatment for pancreatic cancer

- Approximately 20% of patients undergo surgical resection
  - 5-year survival rate: 18-24%
- Generally diagnosed among older adults
  - Median age at diagnosis: 71

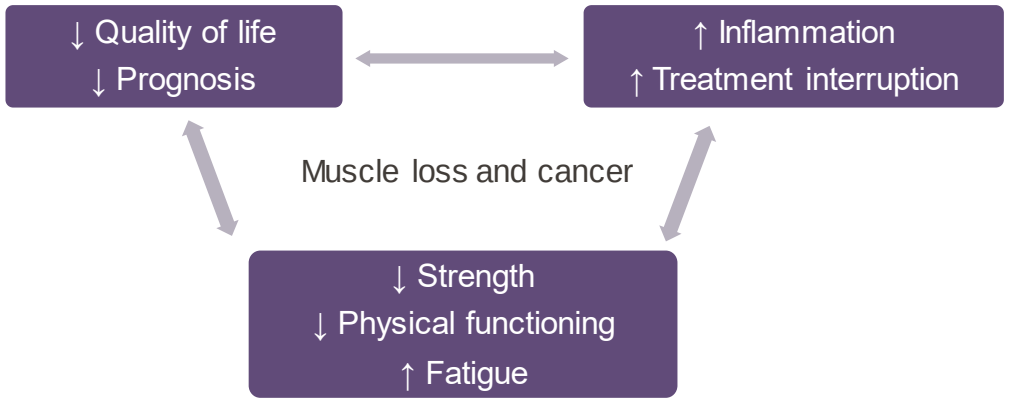
Preoperative treatment context:



(Either treatment or combination of both)

Fitness during preoperative pancreatic cancer treatment

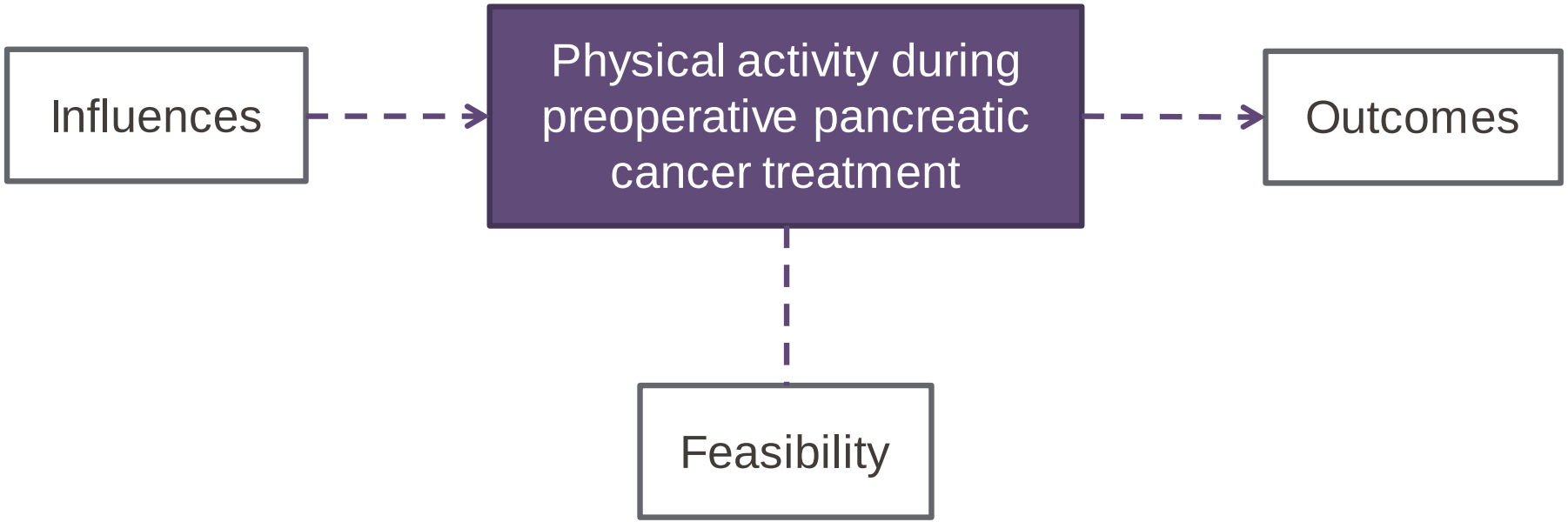
- Muscle loss frequently accompanies preoperative treatment
- Preoperative frailty linked to adverse outcomes following surgery
- **Important to optimize preoperative health!**



Cooper et al., 2015; Cloyd et al., 2018

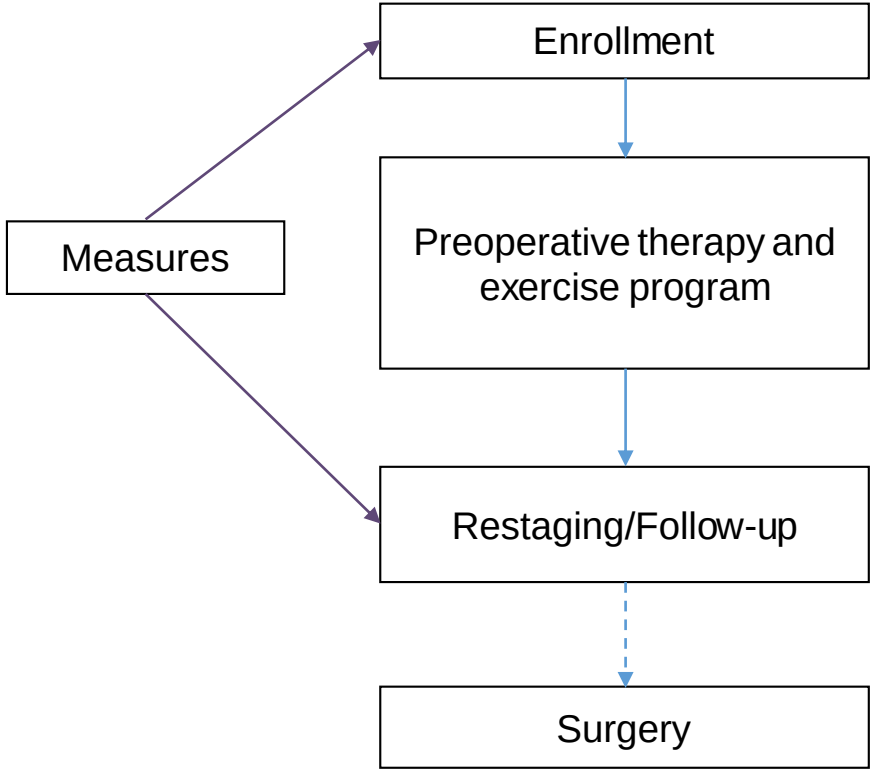
Lee et al., 2018; Broughman et al., 2015

Pancreatic cancer prehabilitation pilot study (2015-2018)



Study design: Participants and study structure

- Single-arm feasibility study
- 50 patients
  - Biopsy-proven pancreatic cancer
  - At least 6 weeks of preoperative treatment before planned surgical resection
- Screened for safety of independent exercise (PAR-Q questionnaire and physician consultations, as necessary)



Study design: Home-based exercise program

- Exercise prescription
  - ≥60 min/week moderate-intensity aerobic exercise
  - ≥60 min/week strengthening exercise

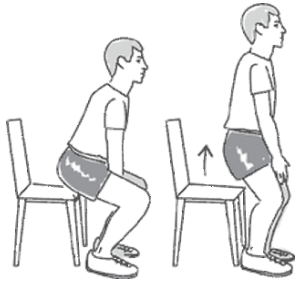
- Participants received
  - Graded resistance tube sets
  - Photo/video instructions
  - Comprehensive instruction at baseline
  - Follow-up calls every two weeks

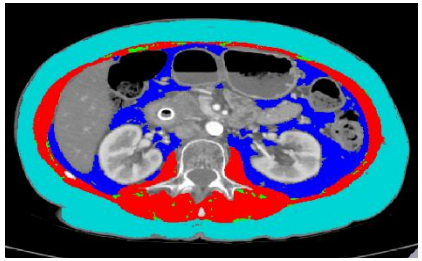
- Physical activity assessed using daily logs and accelerometers

Measures

- **Potential exercise influences (surveys)**
  - Social support from family and friends
  - Perceived walkability of home neighborhoods

- **Potential exercise outcomes (surveys and "field tests")**
  - Physical functioning and fitness
  - Health-related quality of life
  - Skeletal muscle tissue



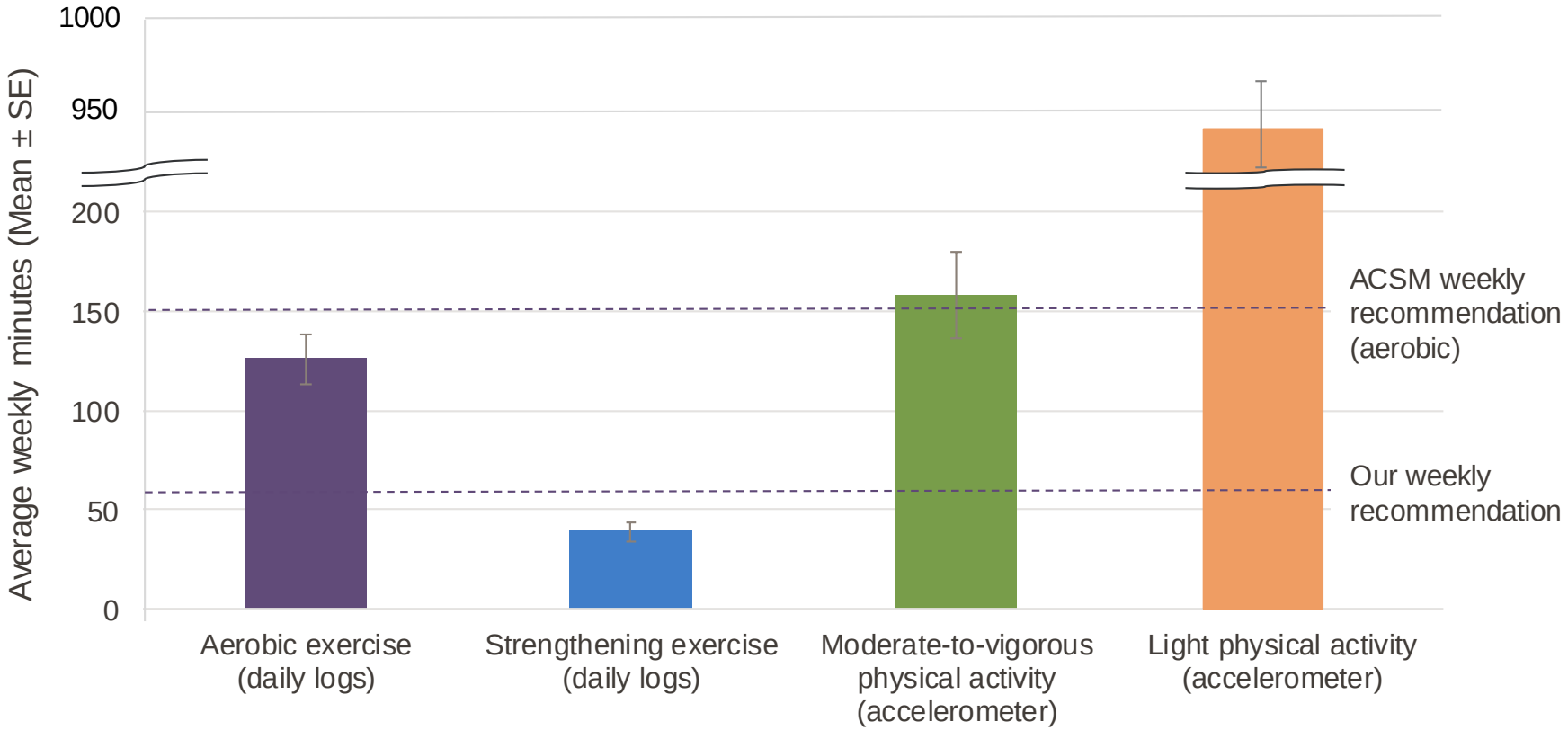


Participant characteristics (*N*=50)

	Value
Mean age at enrollment, years ± SD	66 ± 8
Sex, *n* (%)	
Female	24 (48)
Male	26 (52)
Mean BMI at baseline, kg/m^2 ± SD	27.6 ± 5.3
Normal weight (18.5 ≤ BMI < 25), *n* (%)	18 (36)
Overweight (25 ≤ BMI < 30), *n* (%)	18 (36)
Obese (BMI ≥ 30), *n* (%)	14 (28)
Mean exercise program duration, weeks ± SD	16 (9)

Geographic spread of participants

Self-reported exercise and accelerometer physical activity



Home environment influences on physical activity

More social support for exercise from family and friends

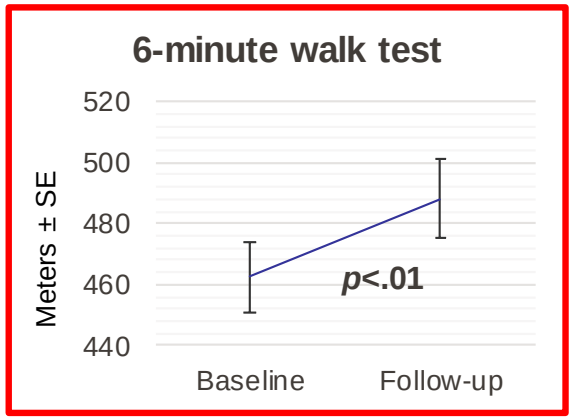
More walkable neighborhoods

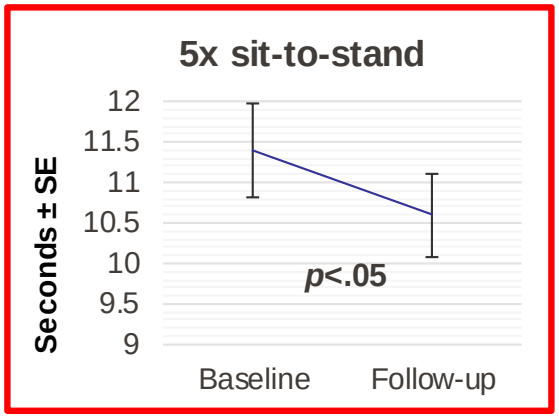
More accelerometer physical activity

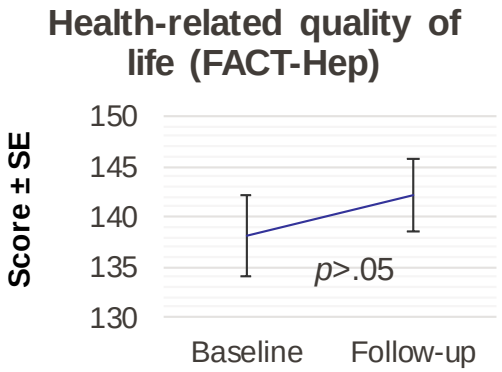
Both $p<.05$

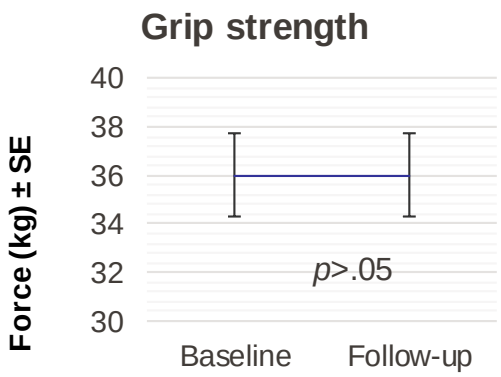
Adjusted for age, sex, and duration of treatment and exercise program.

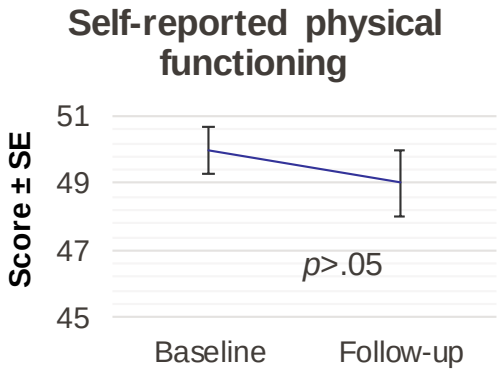
Outcome measures









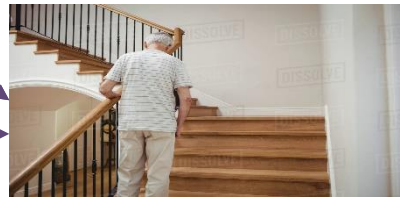


Associations among physical activity and outcomes

More self-reported aerobic exercise

More accelerometer physical activity

Better improvement in 6-minute walk distance

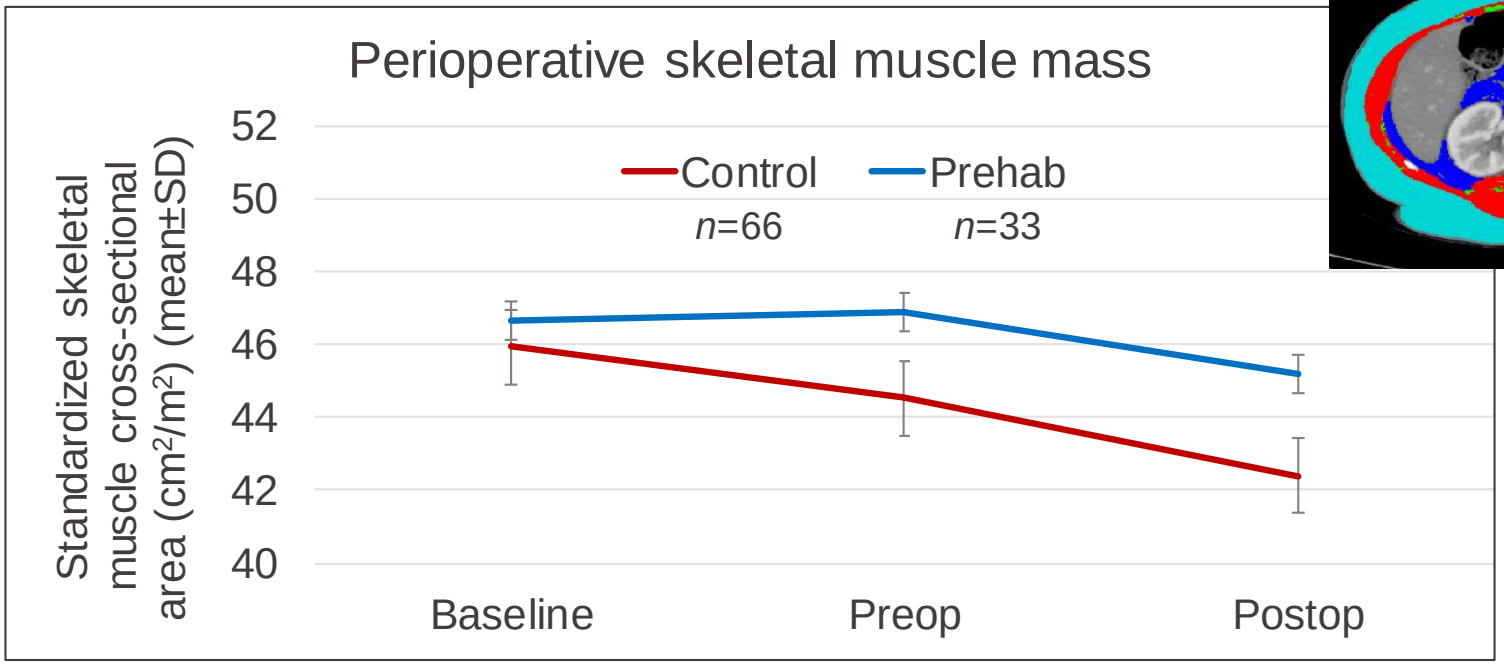


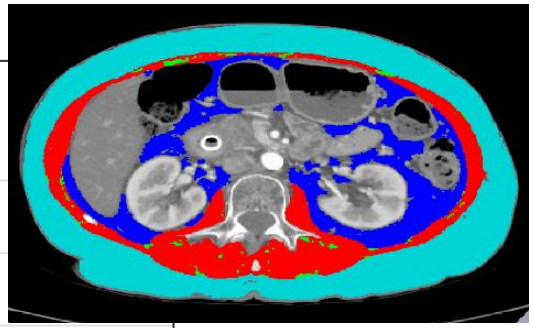
Better improvement in self-reported physical functioning

All $p<.05$

Adjusted for age, sex, duration of treatment and exercise program, and baseline value of the outcome.

Exercise prescription may mitigate muscle loss during preoperative pancreatic cancer treatment





p<.05 for rates of muscle change from baseline to pre-op and baseline to post-op (models adjusted for age, sex, baseline skeletal muscle CSA)

Conclusions from pancreatic cancer prehab study

- **Exercise is feasible during preoperative pancreatic cancer treatment**
  - Capitalizing on high motivation in the preoperative “window”
  - Differences in adherence – due to differences in motivation?

- **Social support and neighborhood walkability may be important exercise influences with home-based exercise prescription**
  - Potential to mitigate barriers and maximize support

- **Exercise during preoperative pancreatic cancer treatment may confer important benefits**
  - Improving fitness and physical functioning
  - Improving health-related quality of life
  - Mitigating muscle loss

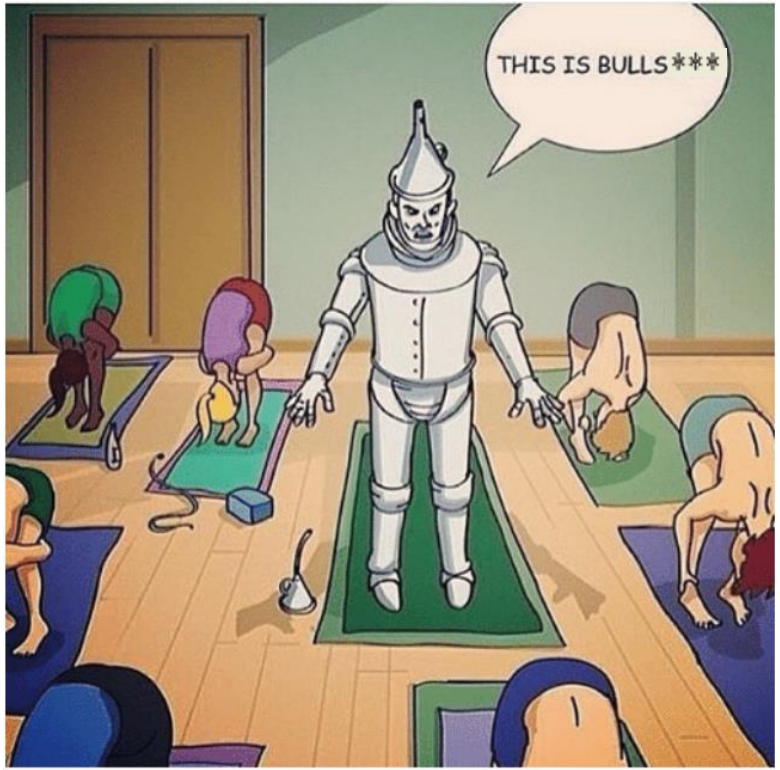
Current research

- "PancFit" randomized trial **(currently accruing patients)**
  - Home-based aerobic and strengthening exercise prescription vs. standard care (general encouragement to exercise)
  - Encouragement to maintain a high protein diet and early dietitian consultation (as needed) for both groups
  - Daily physical activity measured using Fitbit Charge 2 activity monitors
  - Measuring exercise motivation
  - Testing effects of multi-modal exercise on fitness, body composition, quality of life, and vascular remodeling in tumors

fitabase

Potential reasons for subpar adherence resistance training

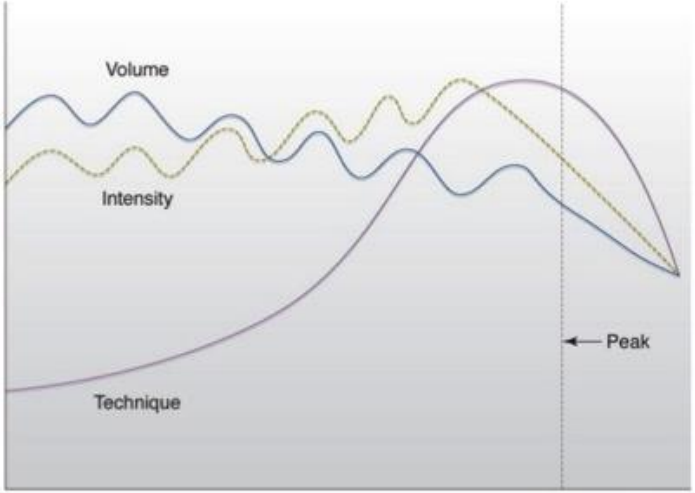
- New exercise modality
  - Lack of self-efficacy
  - Lack of familiarity
- Home-based resistance training program
  - Equipment issues
  - Limited supervision/social support
  - Lack of muscular **overload**
  - Lack of exercise volume **progression**
- Structure of recommendations
  - One size does not fit all
  - Not scheduled (or periodized) to account for treatment or side effects



Resistance training 101

Overload

Place a greater demand on a muscle than it is accustomed to meeting. This leads to muscular hypertrophy and increased strength.



Progression

Increase the demand placed on a muscle over time

Periodization

Vary training volume and intensity systematically to manage fatigue and prevent training “staleness” or “plateaus”

Comparing Resistance Training Intervention Formats

In-person and supervised

- Gold standard in exercise oncology
- Greater control of training variables
- Safety
- Exercise self-efficacy
- Social support of interventionists and other facility users
- Adherence

Home-based and unsupervised

- Lower cost
  - Financial
  - Time
- Comfortable
- Social support of family or caregivers
- Feasibility
- Enrollment/participation

"PancStrength" feasibility study

Primary objective:

Evaluate the **safety** of a progressive, home-based, **tele-exercise resistance training (RT) intervention** in patients undergoing chemotherapy for pancreatic cancer

Secondary objectives:

Evaluate program **feasibility** and **acceptability**

Examine changes in exploratory outcome measures (fitness, clinical, and PROs) and their associations with RT volume

Evaluate cancer care providers' perspectives regarding intervention feasibility and acceptability

“PancStrength” feasibility study

- 25 patients undergoing first-line chemotherapy for pancreatic cancer
- ~30-minute **tele-RT** sessions over one-to-one Zoom video conference with ACSM-certified exercise trainers

- **Progressive and individualized RT program**
  - Starting resistance based on baseline strength
  - Exercise volumes to increase based on perceived exertion
  - Training periodized based on chemotherapy treatments and potential side effects (4 sessions/2 weeks)

Optimizing exercise prehabilitation: future directions

- Applying tele-resistance training to our prehabilitation model
- Study and compare feasibility of in-person training
- Incorporate nutritional intervention and assessment
- Examine effects of prehabilitation on other important outcomes
  - Surgery-related outcomes
  - Return to baseline fitness and physical functioning
  - Mitigation of muscle loss
  - Personalized and tailored intervention for higher-risk groups

Collaborators

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Keri Schadler, PhD

General Internal Medicine
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Funding

- National Institutes of Health (1R21CA218732-01A1, PI Keri Schadler)
- Center for Energy Balance in Cancer Prevention & Survivorship, Duncan Family Foundation
- Knox Family Foundation
- Cancer Prevention & Research Institute of Texas Training Grant/MD Anderson Cancer Prevention Research Training Program

Thank you! Questions?