Reversing Muscle Loss: Exercise

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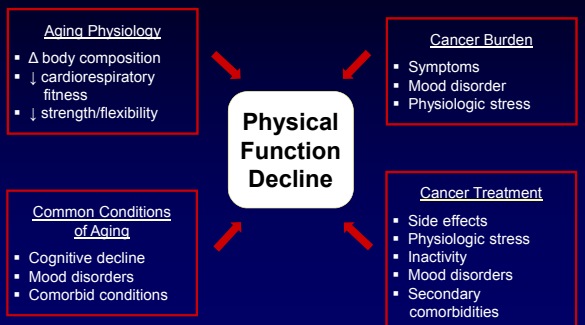
No disclosures

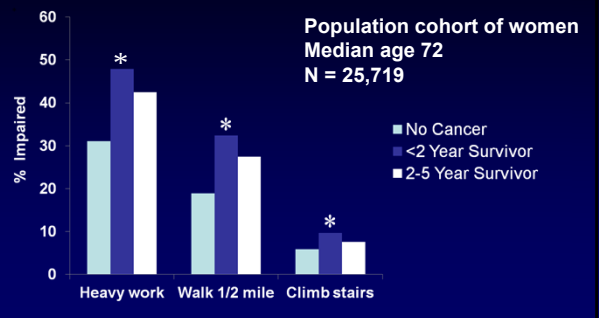
Outline

- The case for exercise
- What do we know about exercise?
  - Older adults without cancer
  - Younger adults with cancer
  - Older adults with cancer
- What do we need to know to change practice?

Older cancer patients are at high risk for functional decline:The perfect storm



The impact of cancer treatment on self-reported physical function



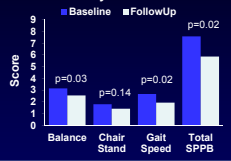
* p<0.05

Sweeney et al. JNCI 2006

The impact of cancer treatment on objective physical function

Older adults with AML-Intensive chemotherapy[1] (N=50)

Declines in Physical Performance



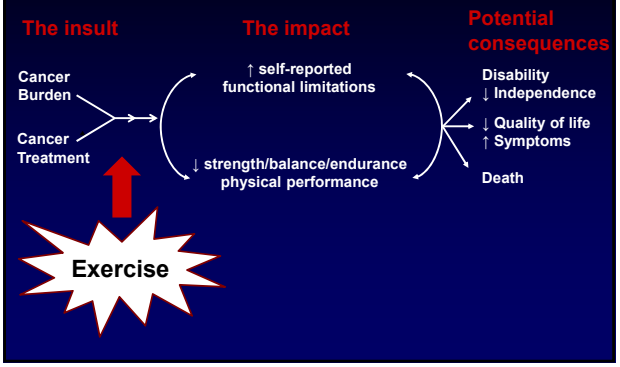
Declines in Strength

Older adults with breast cancer-aromatase inhibition[2] (N=27)

	% change in grip strength over 6 months	P value
Left	**-8.0**	0.009
Right	**-11.4**	0.009

1. Klepin et al. unpublished, SIOG 2012; 2. Lintermans et al. Annals of Oncology 2011

Intervening on the functional decline cascade



Benefits of exercise: non-cancer elderly patients

Populations shown to benefit*
Healthy Community Dwelling[1,2]
Frail Community Dwelling[3]
Institutionalized (Nursing Home)[4]
Chronic Pulmonary Disease[5]
Congestive Heart Failure[6]
Osteoarthritis[7]
Osteoporosis[8]

*representative sample of elders studied in RCT, list if not exhaustive

Positive Functional Outcomes
Lean body mass[9]
Strength
Balance
Performance (ie. walking speed)
Flexibility
Fitness
Self-reported activities (ie. IADLs)

Themes: resistance training→strength; aerobic training→fitness
Limitations: most trials measure short term changes

1. Cress et al. J Biol A Sci Med Sci 1999; 2. Bean et al. Arch Phys Med Rehabil 2004; 3. Chou et al. Arch Phys Med Rehabil 2012; 4. Fiatarone et al. NEJM 1994; 5. Berry et al. J Card Rehab 2003; 6. Kitzman et al. Circ Heart Fail 2010; 7. Ettinger et al. JAMA 1997;8 Howe et al. Cochrane Database Syst Rev 2011; 9 Peterson et al. Med Sci Exerc 2011

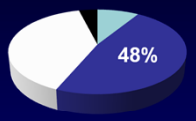
Benefits of exercise in cancer survivors

Systematic review
- 82 trials (90% RCTs)
- Intervention sample size:
  - Mean 42, range 6-319

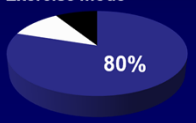
Who was studied?
- 83% breast cancer
- 40% receiving active treatment

Intervention characteristics

Duration of intervention



Exercise mode



60% moderate to vigorous, 3-5 x/week

Speck et al. J Cancer Surviv 2010

Benefits of exercise in cancer survivors: positive effects

Outcomes	Study Type (N=66)[1]	
	Exercise During Treatment	Exercise Post Treatment
Upper extremity strength	↑	↑↑
Lower extremity strength	↑	↑↑
Aerobic fitness	↑	↑
Flexibility	insufficient	insufficient
Balance	Not reported	Not reported

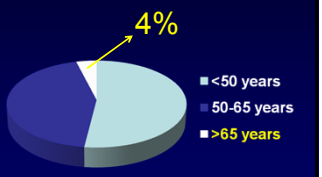
Guidelines: post-treatment survivorship period : ≥30 minutes moderate to vigorous at least 5/week; during treatment: "individualized"[2]

1. Speck et al. J Cancer Surviv 2010; 2. Doyle et. al CA Cancer J Clin 2006

Exercise in older adults with cancer: Data are scarce

- Review of 48 exercise trials for cancer survivors reporting data on age
- None targeted older adults
- 20% used age as an exclusion criteria
- 2 trials enrolled patients ≥75 years of age

Breakdown of mean age reported in exercise trials



Courneya et al. Crit Rev Oncol Hematol 2004

Exercise in older adults with cancer: a focus on prostate cancer

Population	Age	N	Supervised Intervention	Functional Outcomes
Radiation				
Segal[1]	66	121	**Resistance (R) vs. aerobic (A)** vs. usual care (UC) (24 wks)	↑**strength (R only)** ↑ fitness (both)
Monga[2]	68	21	A vs. UC (8 wks)	↑ **strength**, ↑ fitness, ↑flexibility
AST*				
Galvao[3]	70	57	A+R vs. UC (12 wks)	↑**lean mass, ↑strength** ↑ walk time, ↑balance
Bourke[4]	72	50	A+R‡ vs. UC (12 wks)	↑ **strength**, ↑fitness

*AST=androgen suppression therapy; ‡ supervised and self-directed

1. Segal et al. J Clin Oncol 2009; 2. Monga et al. Arch Phys Med Rehabil 2007; 3 Galvao et al. J Clin Oncol 2010; 4. Bourke et al. Cancer Epidemiol Biomarker Prev 2011

Older adults have more to gain: A look at age and outcomes

- Prostate cancer patients on XRT±AST
- RCT: Resistance (R) vs. aerobic (A) vs. usual care (UC)
- N=46 ≤65 years; N=75 >65 years

Difference in outcome over 24 week intervention

	Resistance	Aerobic	Usual Care
Age ≤65 years			
Lean mass	No change	No change	No change
Leg extension	↑	↑	No change
Bench press	↑	No change	No change
Age >65 years			
Lean mass	No change	↓	↓
Leg extension	↑	No change	No change
Bench press	↑	No change	↓

Alberga et al. Support Care Cancer 2012

Elderly specific trials: Few and far between

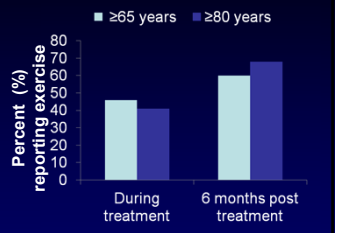
Population	N	Age	Intervention	Objective Results
Targeting Age >50				
Breast cancer[1] (post treatment)	106	62	Resistance+impact versus flexibility (control)	↑lean mass
Acute myeloid leukemia[2] (during chemotherapy)	24	65	Combined modality (non-randomized)	↑ physical performance (NS)
Targeting Age >60				
Locally advanced solid tumor[3] (post treatment)	20	75	12 wk supervised LE resistance exercise (non-randomized)	↑ knee extension peak torque ↑ TUG

Legend:
NS=not statistically significant
LE= lower extremity
TUG=Timed up and Go

1. Winters-Stone et al. Breast Cancer Res Treat 2011; 2. Klepin et al. J Geriatr Oncol 2011; 3. LaStayo et al. J Geriatr Phys Ther 2010

Taking a step back: Are older adults open to physical activity?

- Prospective survey
- 408 newly diagnosed cancer patients with planned treatment
- ≥65 years of age
- Outcomes:
  - Exercise participation
  - Symptoms
  - Self-rated health (SRH)



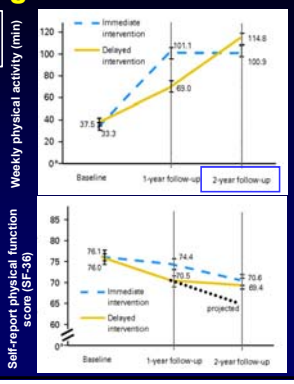
Positive associations among oldest patients:
Exercise during treatment: ↓memory loss, ↓fatigue, ↑SRH
Exercise post treatment: ↓fatigue, ↓ symptom burden

Sprod et al. J Geriatr Oncol 2012

Can physical activity behavior be modified among older adults?

Reach out to enhance wellness (RENEW)

- Randomized trial (N=641)
- Sedentary cancer survivors
- ≥65 years old (mean 73)
- Home-based diet and exercise intervention via print materials and phone
- 1 year duration
- Immediate versus delayed
- Outcomes:
  - -Self-reported physical function
  - -physical activity



Demark-Wahnefried W et al. JCO 2012;30:2354-2361
JOURNAL OF CLINICAL ONCOLOGY

Challenges and unanswered questions

Challenges	Evidence	Limitations/Gaps/Opportunities
Safety	No adverse safety signal	•Few elderly represented •Comorbidity exclusions/frailty •During treatment interventions scarce
Recruitment	Ranges widely (29-86%)	•Often not reported •Factors associated with successful recruitment largely unknown
Adherence	Participation and attrition problems in high risk populations	•Not consistently reported •Strategies to maximize unknown
Intervention	Resistance training has consistent positive effects on strength	•Optimal modality, intensity, frequency and timing? •Supervised versus home-based? •How to individualize? **•What outcomes???**
Durability	Change in physical activity behavior persists 2 years post intervention[1]	•Most interventions <6 months • Longer term effects on function unknown •Sustainability-resources, social support

1. Demark-Wahnefried et al. J Clin Oncol 2012

Conclusions

- Exercise holds promise to attenuate declines in physical function after cancer diagnosis for older adults
- Elderly-specific trials are lacking
- Studies of practical interventions adaptable to heterogenous elderly populations are needed to provide guidance for translation into clinical practice