Exercise Before, During, and After Therapy: How Much Should the Cancer Patient Do?

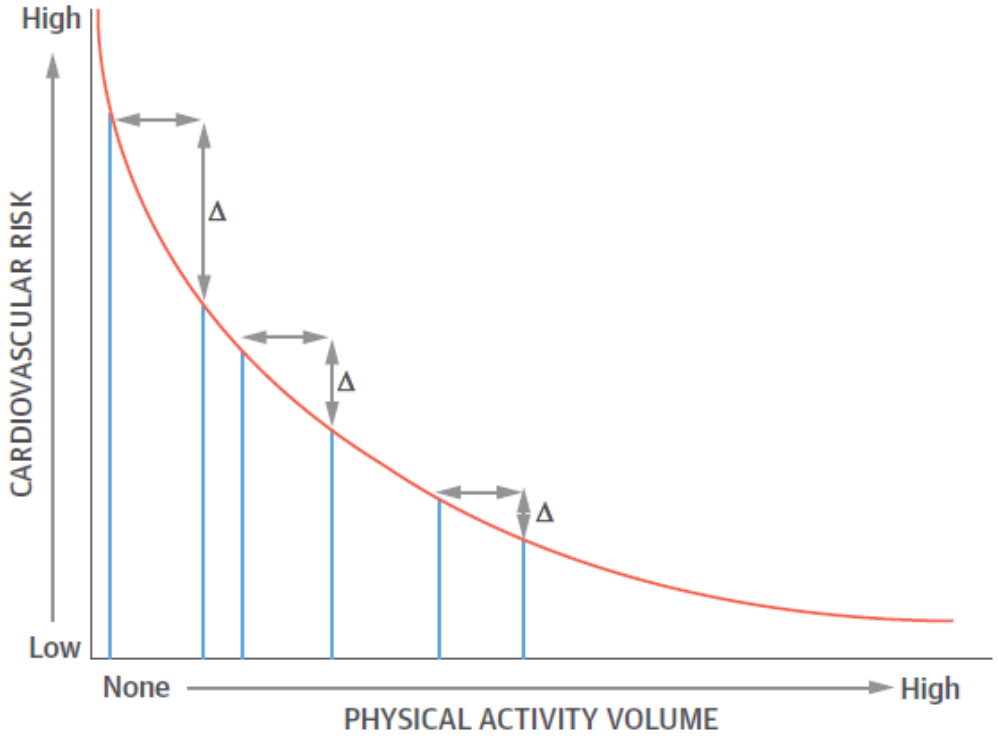
Matt Ehrhardt, MD, MS

AMERICAN COLLEGE *of* CARDIOLOGY

Outline

- Benefits of exercise and fitness
- Cardiovascular risk in cancer survivors
- Safety and efficacy of exercise in cancer survivors
- Recommendations

Physical Activity and Cardiovascular Risk



Eijsvogels et al, *J Am Coll Cardiol* 2016

AMERICAN COLLEGE *of* CARDIOLOGY

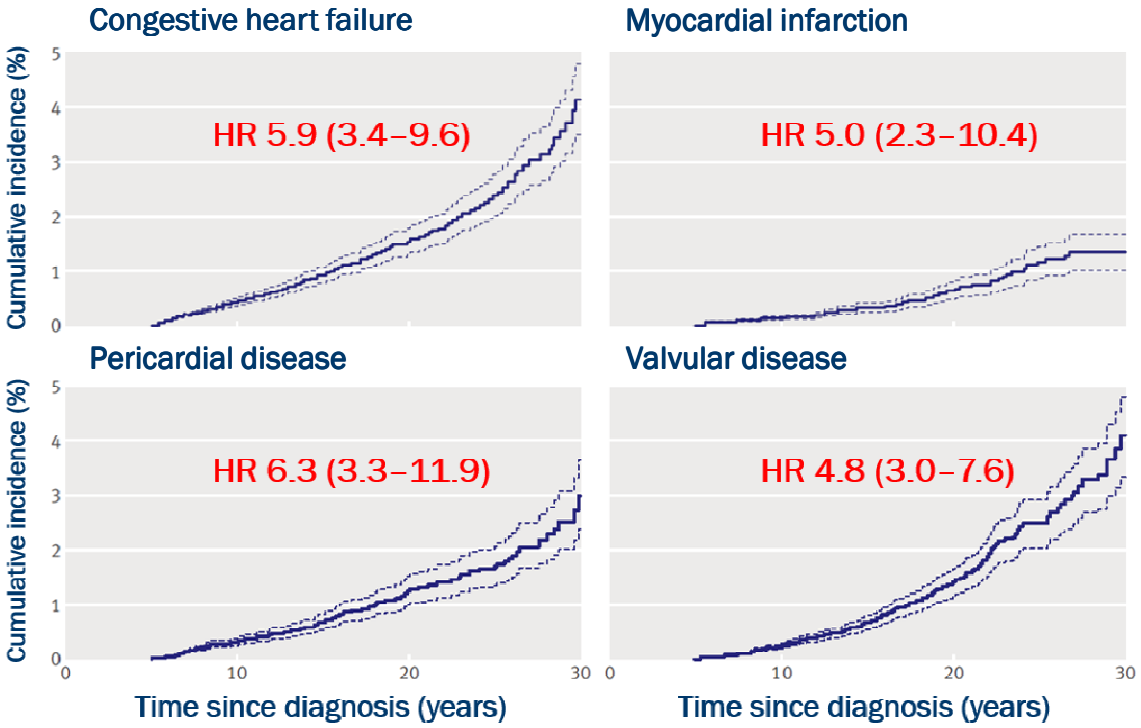
Exercise Also Improves…

- Muscle strength (Behringer et al, *Pediatrics* 2010)
- Bone density (Meyer et al, *Bone* 2011)
- Cognitive function (Angevaren et al, *Cochrane Database Syst Rev* 2008)
- Cardiopulmonary fitness (Ross et al, *Circulation* 2016)

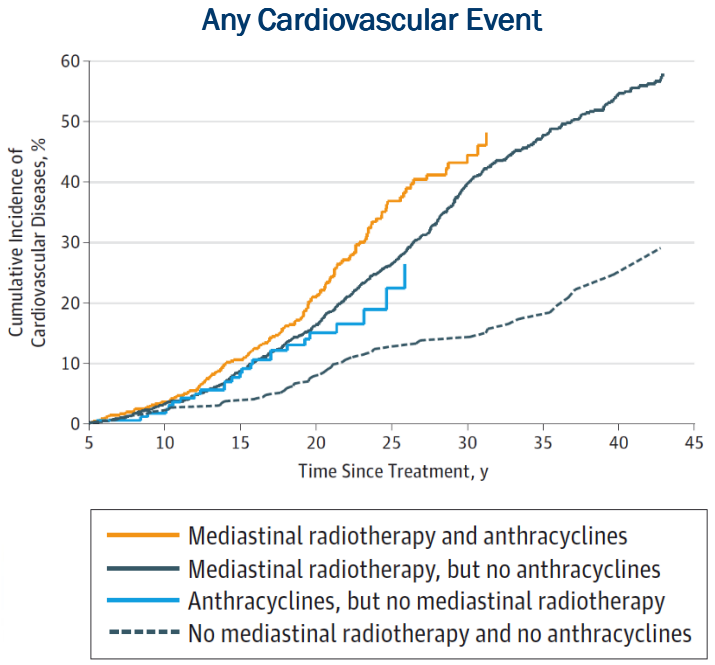
Benefits of Fitness

- 20% decrease in 5-year all cause mortality for each 5 kilogram increase in hand grip strength (Sasaki et al, *Am J Med* 2007)
- 13% decrease in all cause mortality and 15% decrease in cardiovascular disease for each one metabolic equivalent of increased exercise capacity (Kodama et al, *JAMA* 2009)
- 17% increase in total mortality and 13% increase in cardiovascular disease for each one standard deviation decrease in BMD (Qu et al, *Int J Cardiol* 2011)
- Fit adolescents are more than twice as likely to score in the highest tertile of academic achievement than those who are unfit (Sardinha et al, *BMC Pediatr* 2014)

Cardiovascular Risk in Cancer Survivors



Mulrooney et al, *Br Med J* 2009



van Nimwegen et al, *JAMA Intern Med* 2015

Cardiovascular Risk in Cancer Survivors

- Reduced physical function at all levels of physical activity (Hoffman et al, *J Clin Oncol* 2013)
- Exercise capacity (VO_2 max) reduced in many childhood cancer survivors (Berkman, *J Adolesc Young Adult Oncol* 2016)
- Metabolic syndrome more prevalent in cancer survivors than in the general population (de Haas et al, *Lancet Oncol* 2010)
- Multiplicative interaction between CV risk factors and cancer treatment-related exposures (Armstrong, et al *J Clin Oncol* 2013)

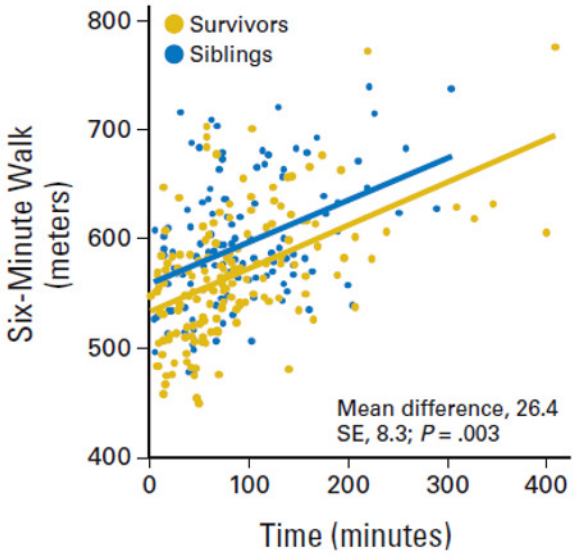
AMERICAN COLLEGE of CARDIOLOGY

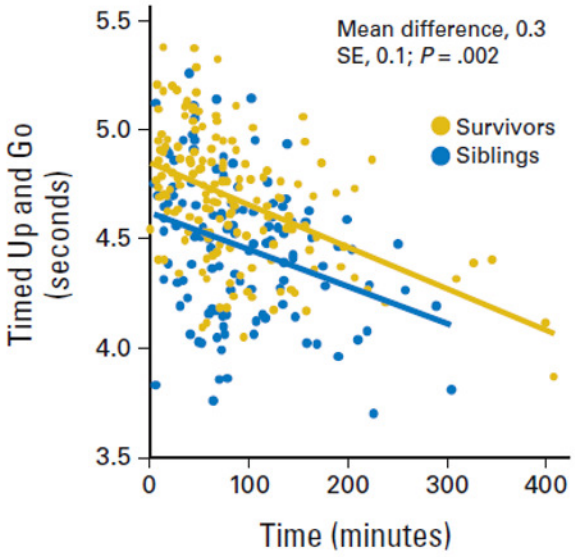
Physical Function in Cancer Survivors

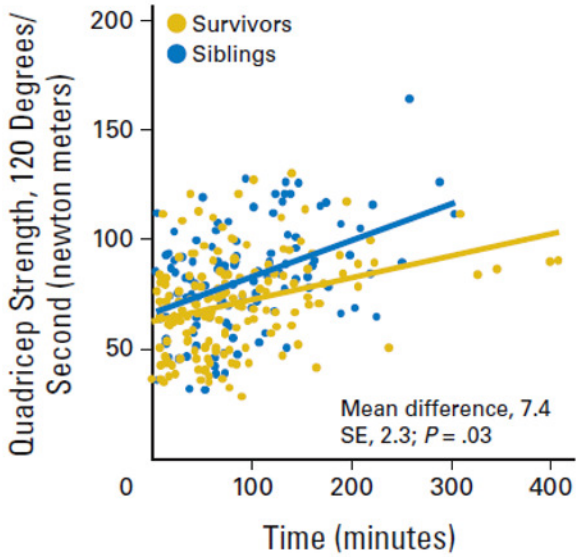
- Childhood Cancer Survivor Study (CCSS)
- 183 young adults (53% male)
  - Mean age at cancer diagnosis 4.2 +/- 3.0 years
  - Mean age at evaluation = 13.5 +/- 2.5 years
  - Evaluated between 2007 and 2010
- Physical function assessment
  - Lower extremity strength: isokinetic dynamometer
  - Grip strength: handheld dynamometer
  - Cardiopulmonary fitness: 6-minute walk test
  - Mobility: timed up-and-go test

Hoffman et al, *J Clin Oncol* 2013

Physical Function in Cancer Survivors



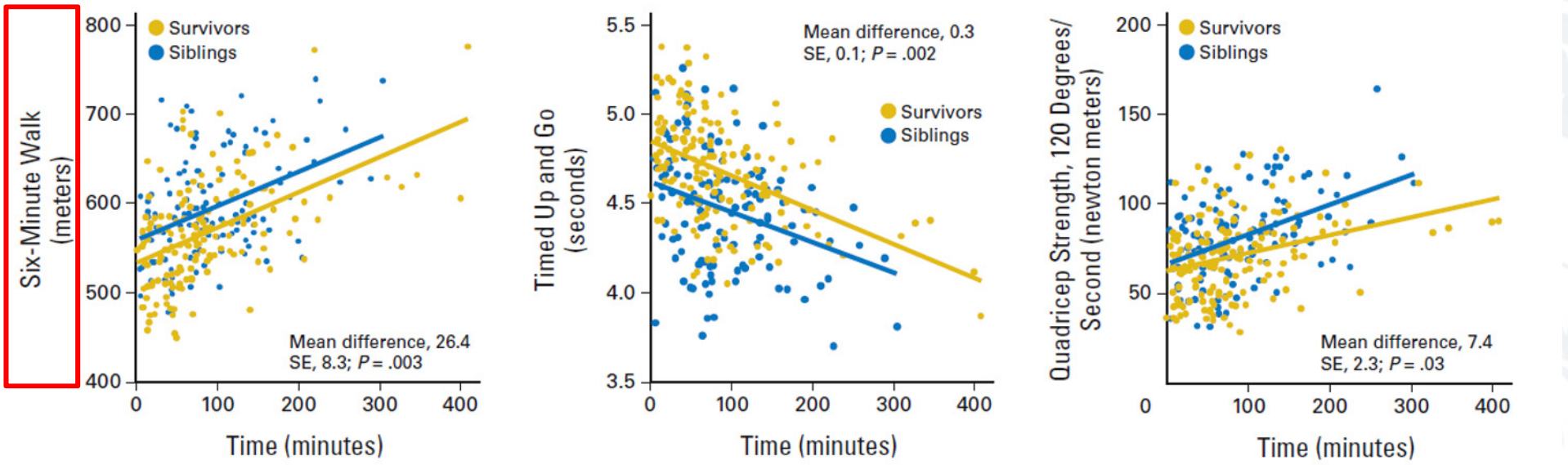




Hoffman et al, *J Clin Oncol* 2013

AMERICAN COLLEGE of CARDIOLOGY

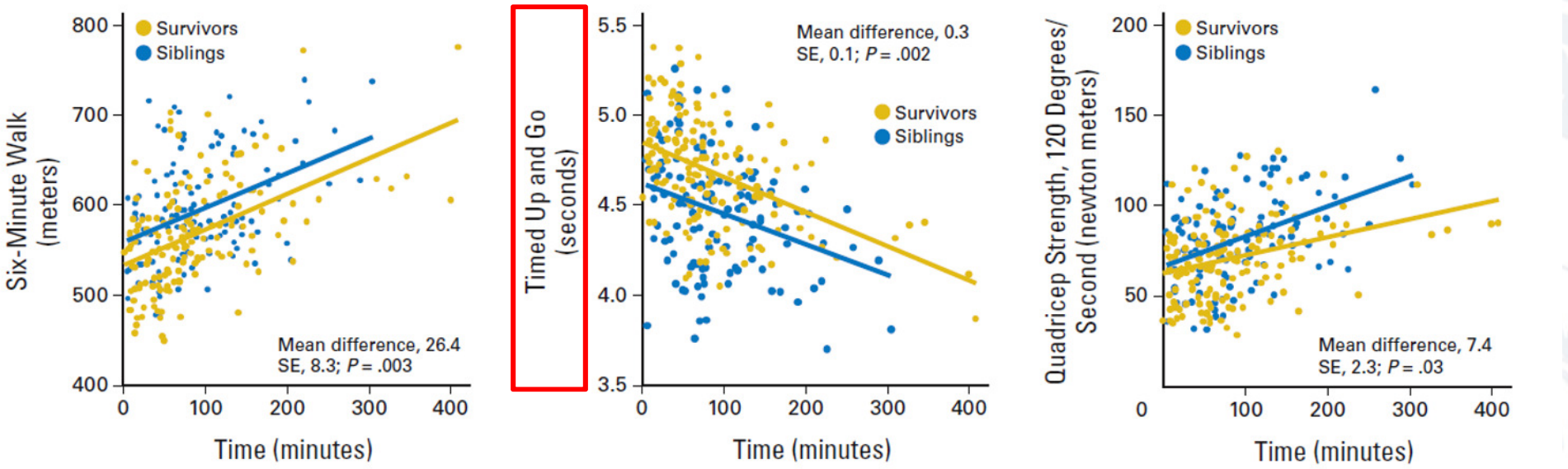
Physical Function in Cancer Survivors



Hoffman et al, *J Clin Oncol* 2013

AMERICAN COLLEGE of CARDIOLOGY

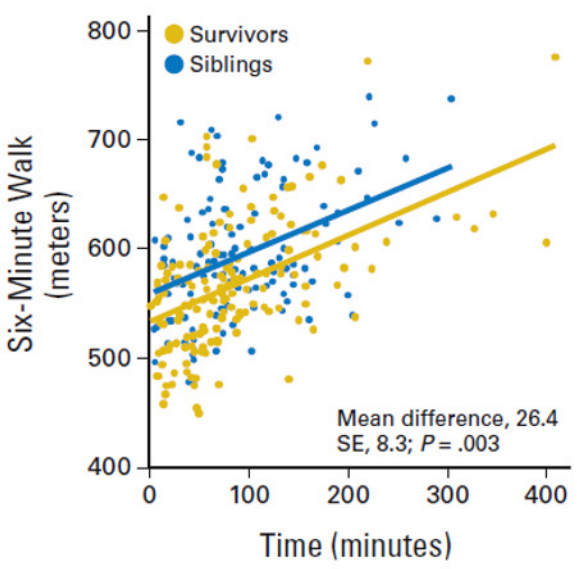
Physical Function in Cancer Survivors

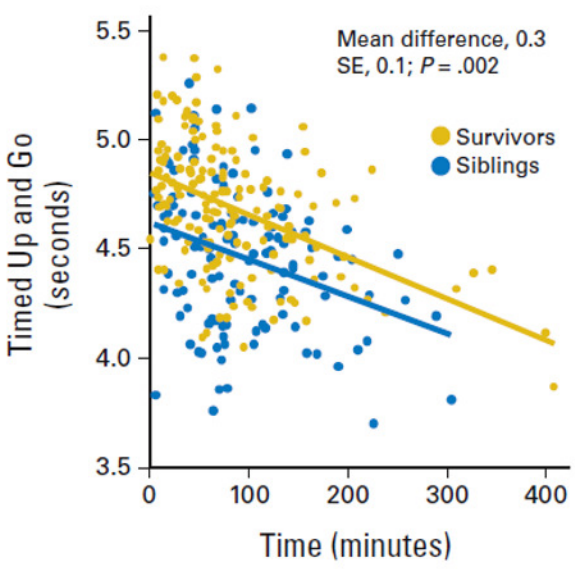


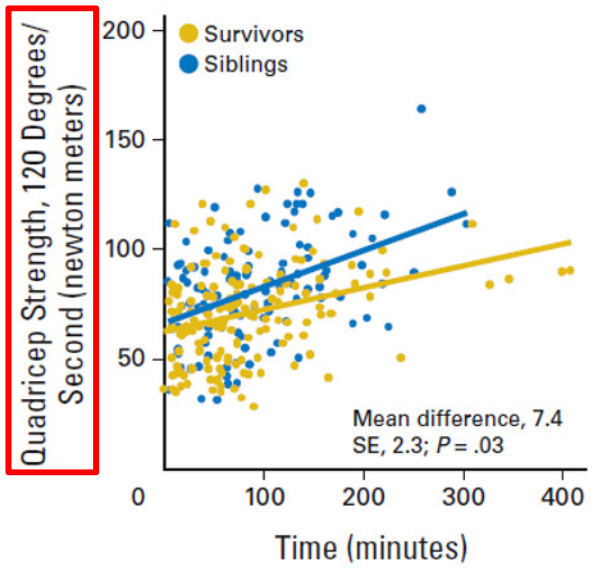
Hoffman et al, *J Clin Oncol* 2013

AMERICAN COLLEGE of CARDIOLOGY

Physical Function in Cancer Survivors





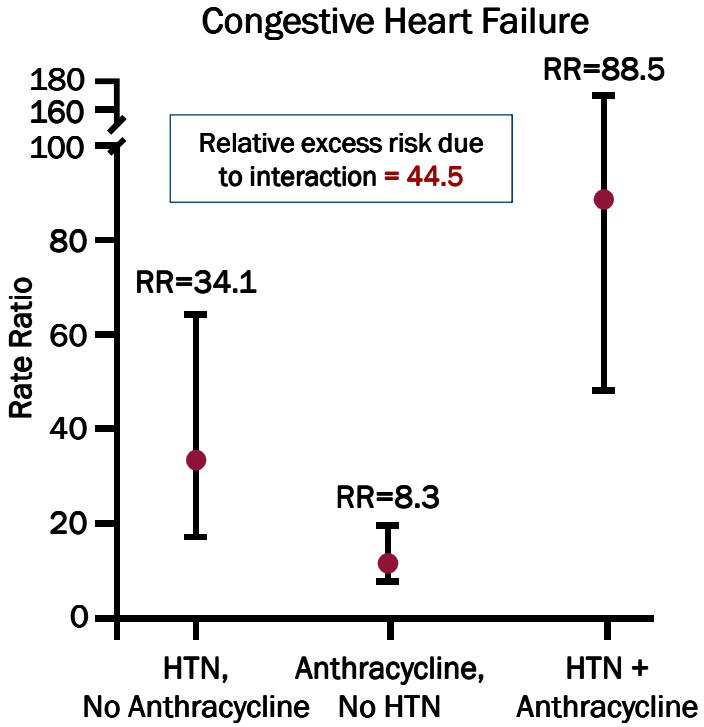


Hoffman et al, *J Clin Oncol* 2013

AMERICAN COLLEGE of CARDIOLOGY

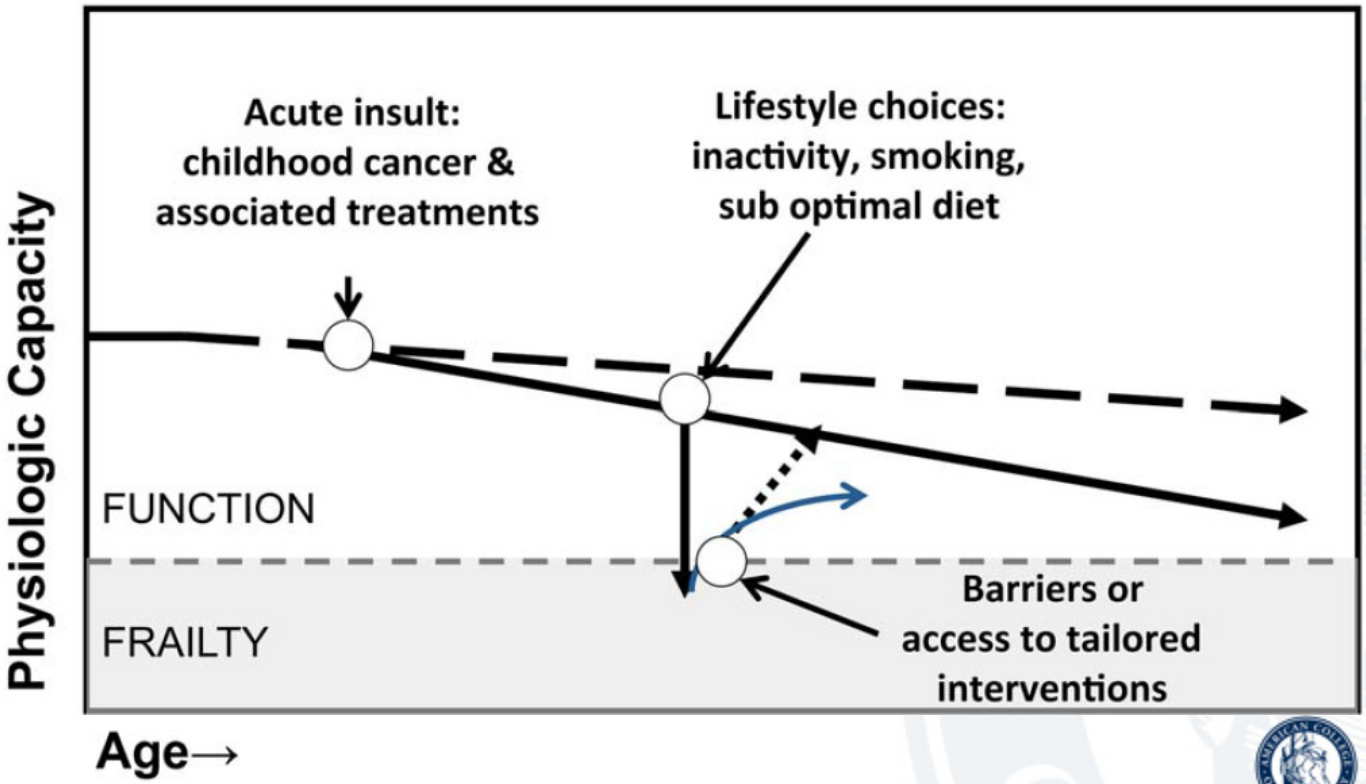
Traditional CV Risk Factors Potentiate Treatment-Related CV Risk

- Evaluate relative contribution of CV risk factors towards CHF
  - Longitudinal evaluation
  - 10,724 survivors, CCSS
  - Is risk simply additive?
  - Hypertension potentiates anthracycline-associated risk for CHF
  - Multiple traditional CV risk factors increase risk



Armstrong et al, *J Clin Oncol* 2013

Modifying Risk in Survivors



Ness et al, *Cancer* 2014

AMERICAN COLLEGE *of* CARDIOLOGY

Modifying Outcome Specific Risks in Survivors

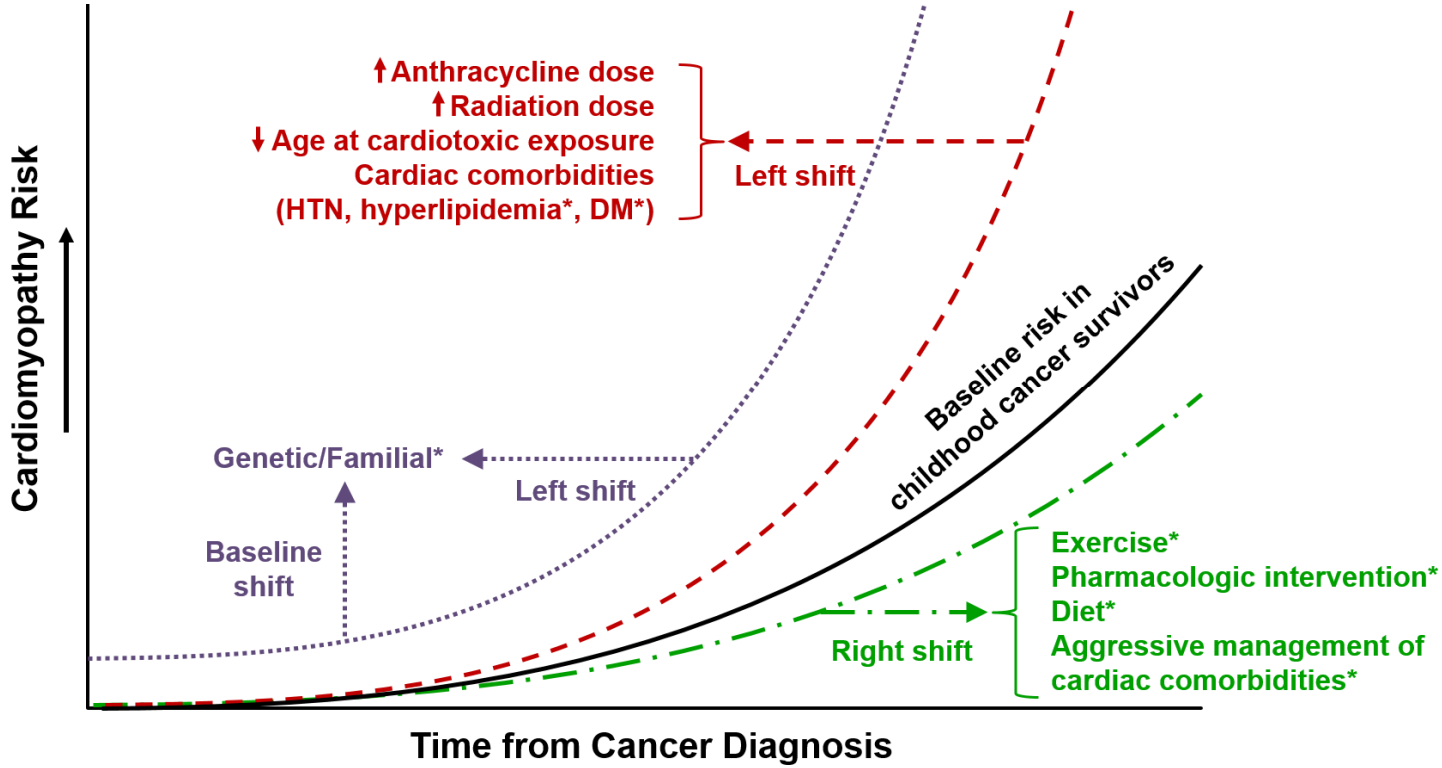


Figure 1. Conceptual schematic of cardiomyopathy risk and modifiers in childhood cancer survivors. Factors designated by an * are under active investigation (knowledge gaps). HTN = hypertension, DM = diabetes mellitus.

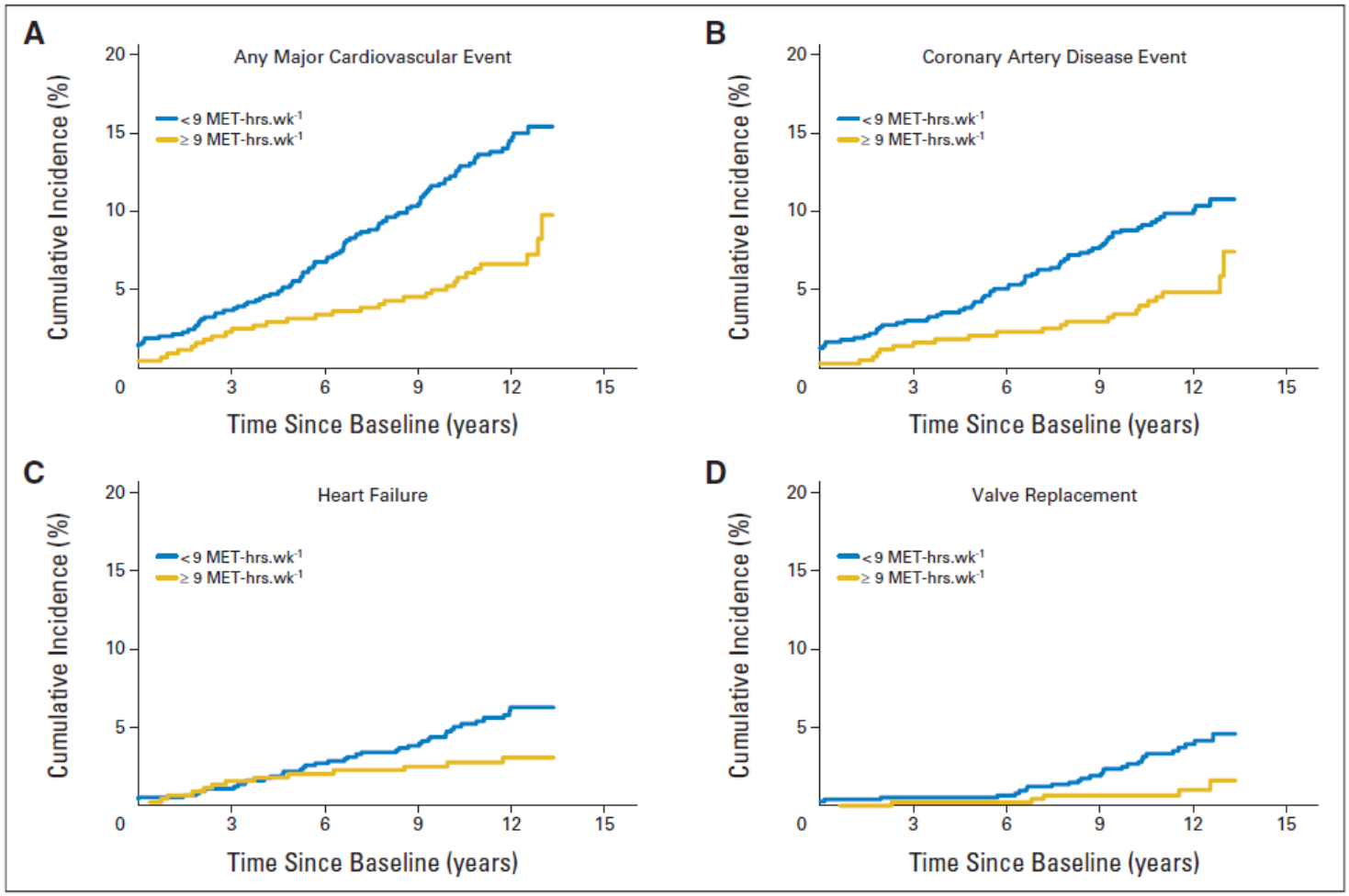
Ehrhardt, Fulbright, Armenian, *Curr Oncol Rep* 2014

AMERICAN COLLEGE *of* CARDIOLOGY

Physical Activity and CV Risk

- Childhood Cancer Survivor Study (CCSS)
- 1,187 survivors of pediatric Hodgkin lymphoma (53% male)
  - Mean age (range) – at diagnosis = 14 years (2-21); at evaluation = 41 years (21-57)
  - Evaluated between 2007 and 2010
  - Modifiable CV risk factors: diabetes (4.4%), hypertension (24.8%), dyslipidemia (18.9%), obesity (20.1%), any of the preceding (43.6%)
  - Treatment related CV risk factors: anthracyclines <250 mg/m^2 (11%), ≥250 mg/m^2 (7.8%), chest RT >30 Gy (83.5%)
- Primary endpoint were CTCAE grades 3-5 CV events
- Exposure to vigorous intensity exercise via validated questionnaire

Jones et al, *J Clin Oncol* 2014



Jones et al, *J Clin Oncol* 2014

Safety

- Tailored intervention is feasible and safe in survivors exposed to anthracyclines with reduced ejection fractions (40-55%) (Smith et al, *Pediatr Blood Cancer* 2014)
- Exercise appears to be safe during breast cancer therapy (Markes et al, *Cochrane Database Syst Rev* 2006)

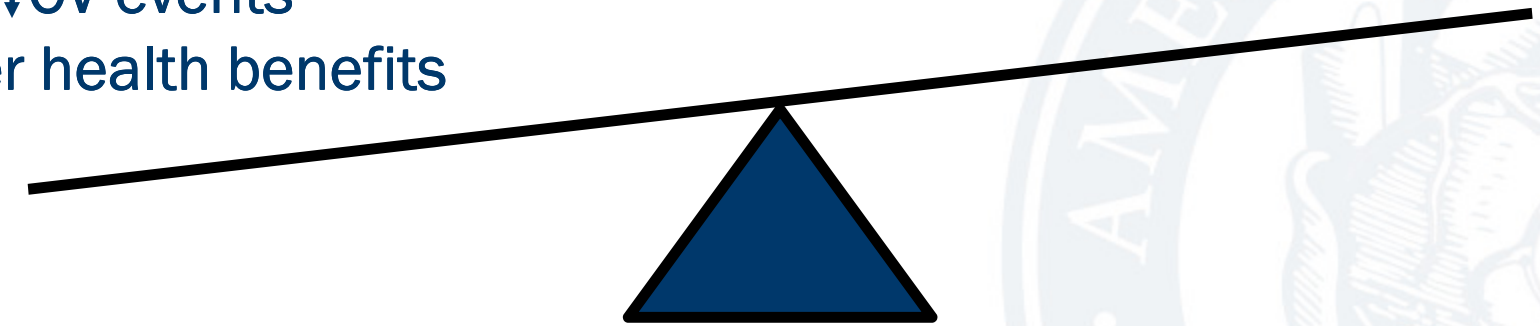
Efficacy

- Exercise improves quality of life, cardiorespiratory fitness, physical function, and fatigue (McNeely et al, *CMAJ* 2006)
- Exercise is feasible and may provide physiological and psychological benefits (Spence et al, *Cancer Treat Rev* 2014; Sharkey et al, *Am J Cardiol* 1993)
- Exercise during breast cancer treatment improves fitness (Markes et al, *Cochrane Database Syst Rev* 2006)
- Exercise during leukemia treatment is feasible and may improve physical function (Esbenshade et al, *Pediatr Phys Ther* 2014)

Weighing the Evidence

<u>Evidence supporting</u>
↓CV risk factors
↓CV events
Other health benefits

<u>Questions regarding</u>
Adverse events



AMERICAN COLLEGE of CARDIOLOGY

Exercise Recommendations

- Regular exercise, as recommended by the AHA and ESC, offers potential benefits to survivors treated with anthracyclines or chest radiation
- Regular exercise is recommended for survivors treated with anthracyclines or chest radiation with normal left ventricular systolic function
- Cardiology consultation is recommended for survivors with asymptomatic cardiomyopathy to define limits and precautions for exercise
- Cardiology consultation may be reasonable for high risk survivors who plan to participate in high intensity exercise to define limits and precautions for physical activity

Armenian et al, *Lancet Oncol* 2015

AMERICAN COLLEGE *of* CARDIOLOGY

Specifically

- ≥150 min/week of moderate-intensity or ≥75 min/week of vigorous-intensity physical activity (ACC, AHA, ACSM, and ECS)
- 2-3 sessions/week of strength training (NCCN)
- Exercise should be tailored to cancer survivor's individual abilities and preferences (NCCN)

Summary

- Survivors incur both cancer treatment-related and traditional cardiovascular risk factors
- Exercise can be safely and efficaciously prescribed
- Cardiology consultation is recommended for survivors at high risk for cardiovascular events in order to define optimal exercise regimens

AMERICAN
COLLEGE *of*
CARDIOLOGY