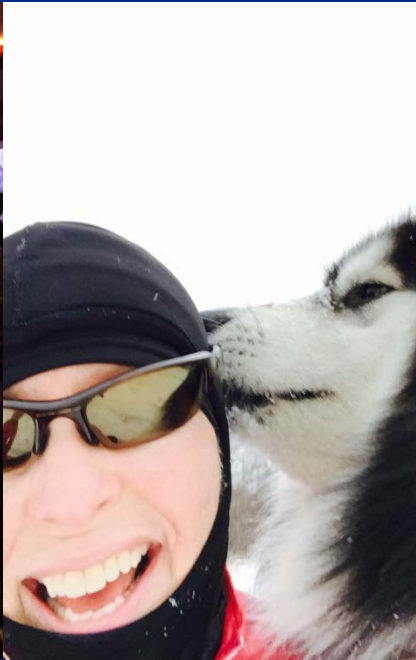




# Effects of Physical Activity on the Heart

Sharon L. Mulvagh MD FACC FASE FAHA FRCP(C)  
Professor of Medicine  
Director, Women's Heart Clinic  
Associate Director, Preventive Cardiology  
Mayo Clinic  
Rochester MN, USA

# Disclosures



*I love running!*

# Learning objectives

- Review the effects of physical activity on the heart and cardiovascular system
- Understand the current debate regarding “dose” of exercise
- Provide guidelines for current patient recommendations

## Question:

Do you try to exercise vigorously at least 3 days per week or accumulate at least 30 minutes of moderate physical activity per day?

# Does Exercise Prevent Cardiovascular Disease over a Lifetime in Healthy People?



Harriette Thompson; 92 yo female completed San Diego Rock 'n Roll Marathon 2015  
Time: 7:24:36

- This is principally an epidemiologic question
- Large, long-term randomized clinical trials are not feasible

# CHD and Physical Activity of Work

CORONARY HEART-DISEASE AND  
PHYSICAL ACTIVITY OF WORK  
J. N. MORRIS      J. A. HEADY  
Lancet 1953



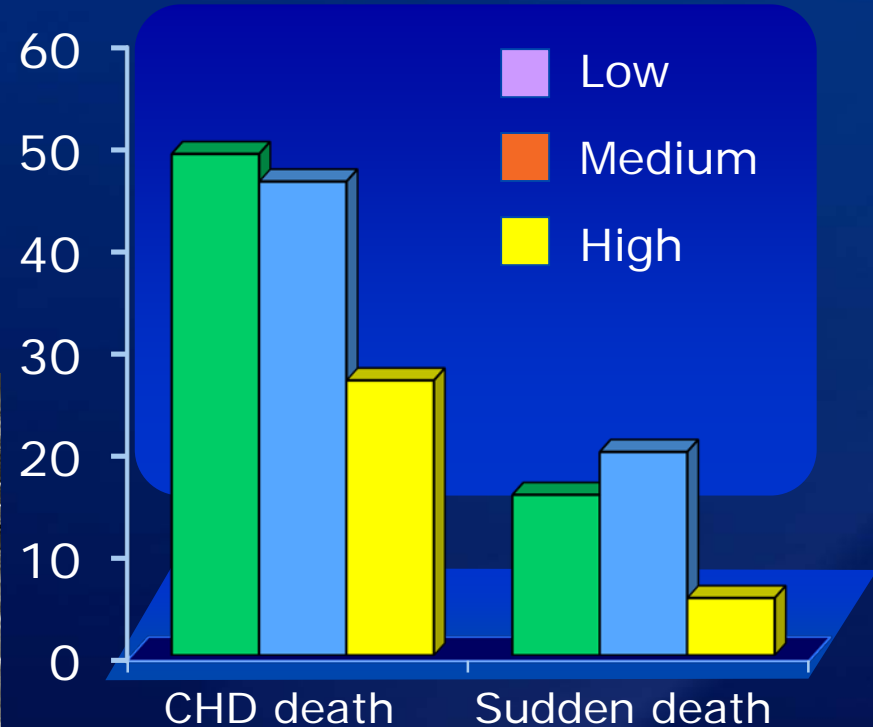
Driver



Conductor

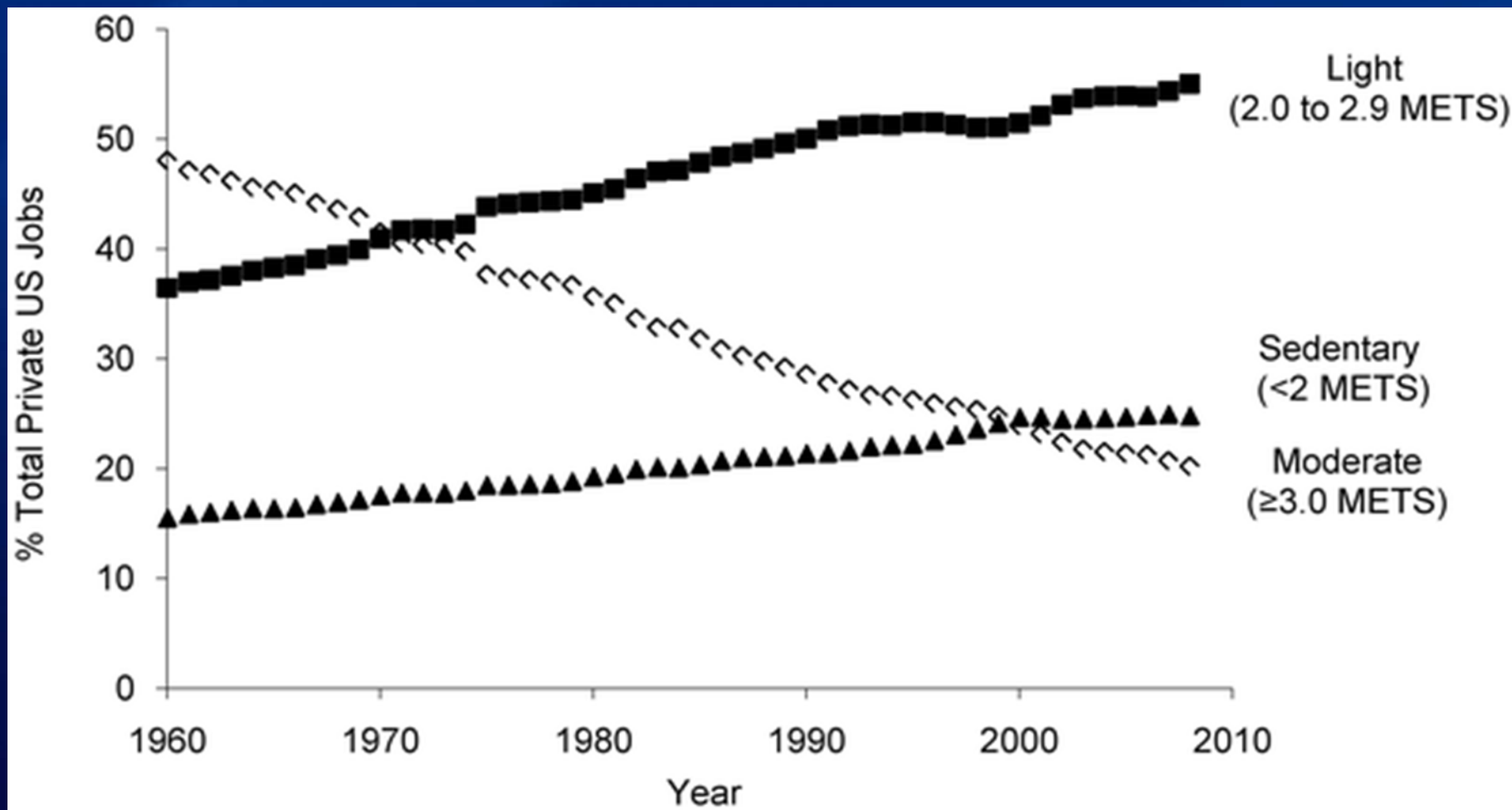


Physical Activity at Work and CHD Deaths in 6,451 Longshoremen



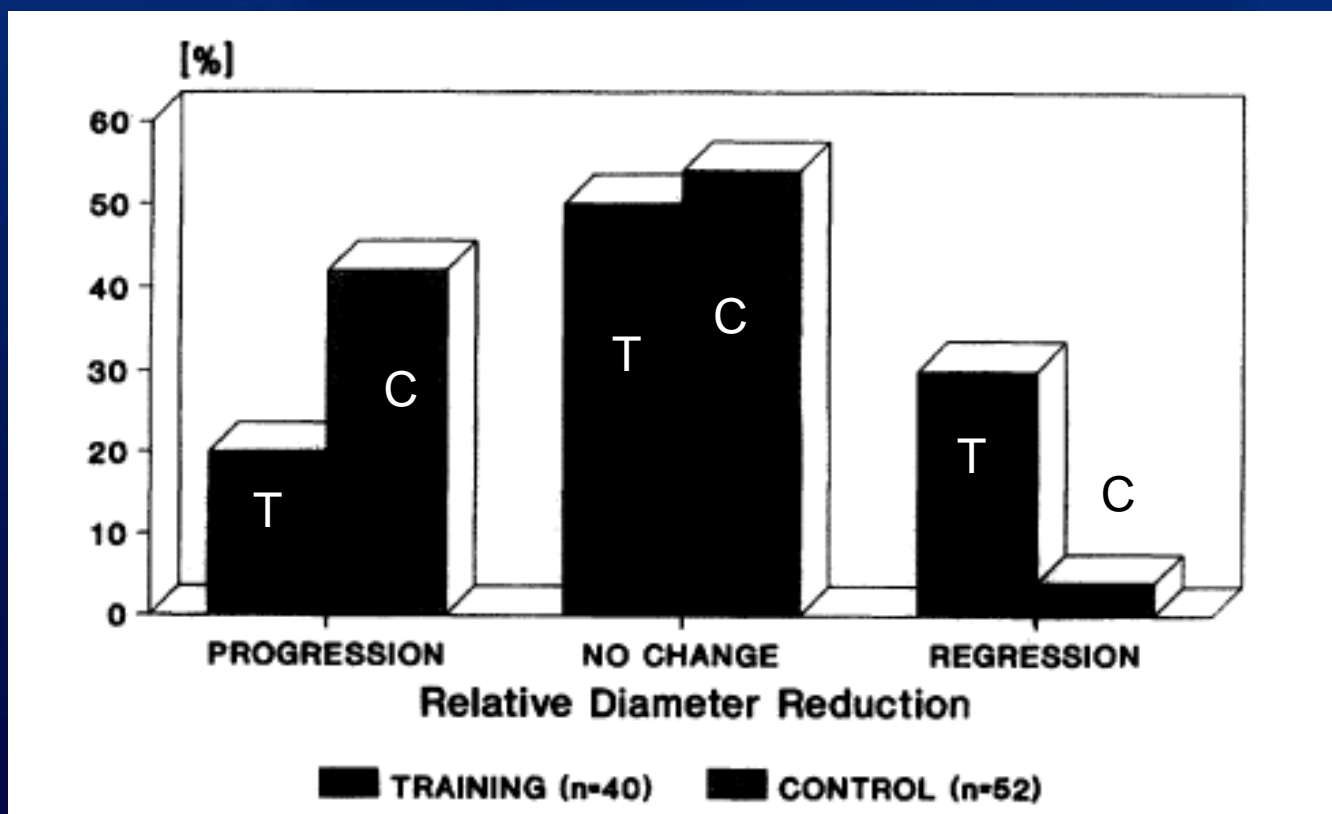
Paffenbarger RS et al. *N Engl J Med.* 1975;292:545-550.

# Occupational Activity 1960-2010



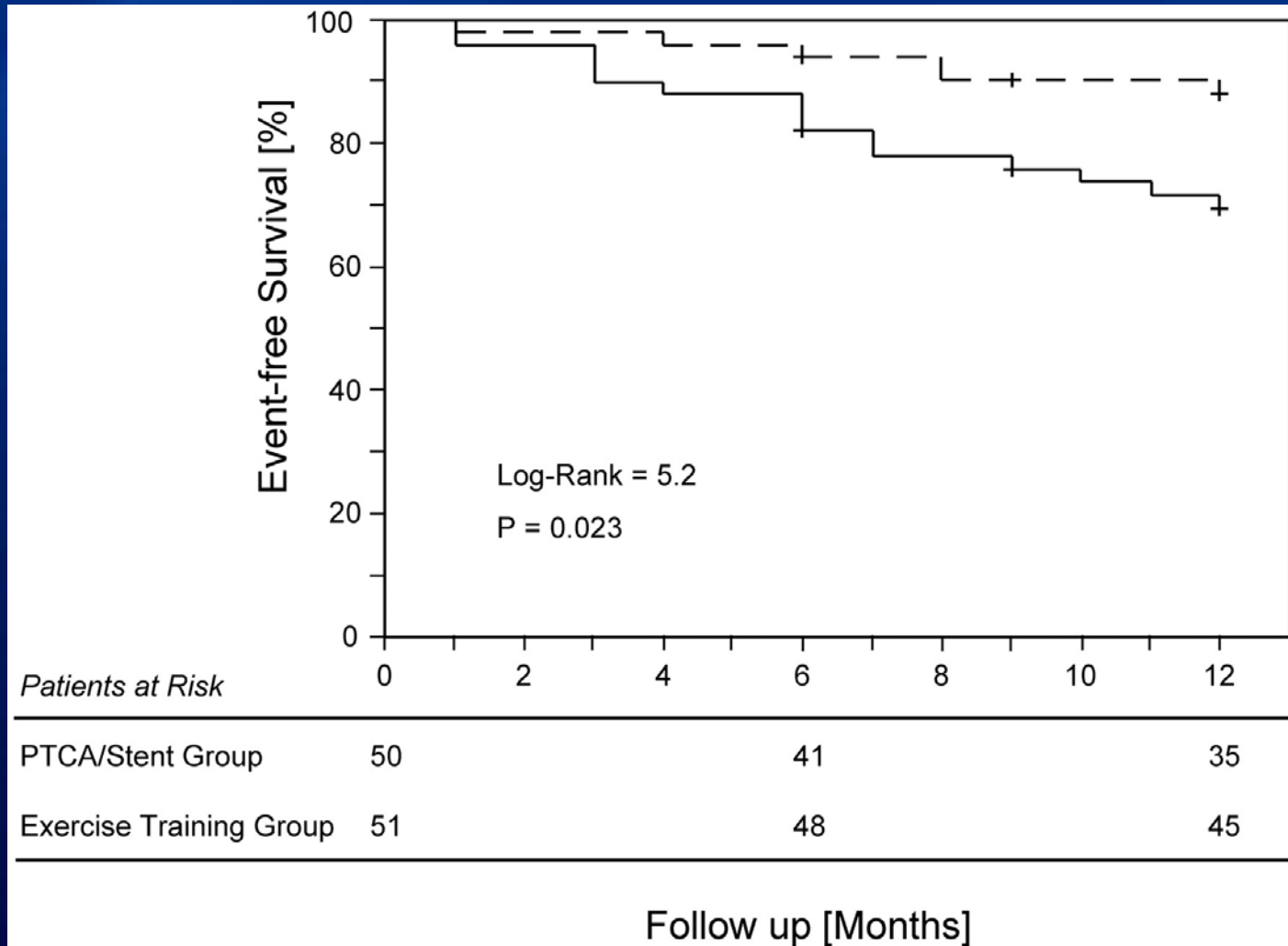
# Effect of Exercise on Coronary Artery Disease Progression

- 113 patients with stable angina randomized
- 12 month training program versus usual care



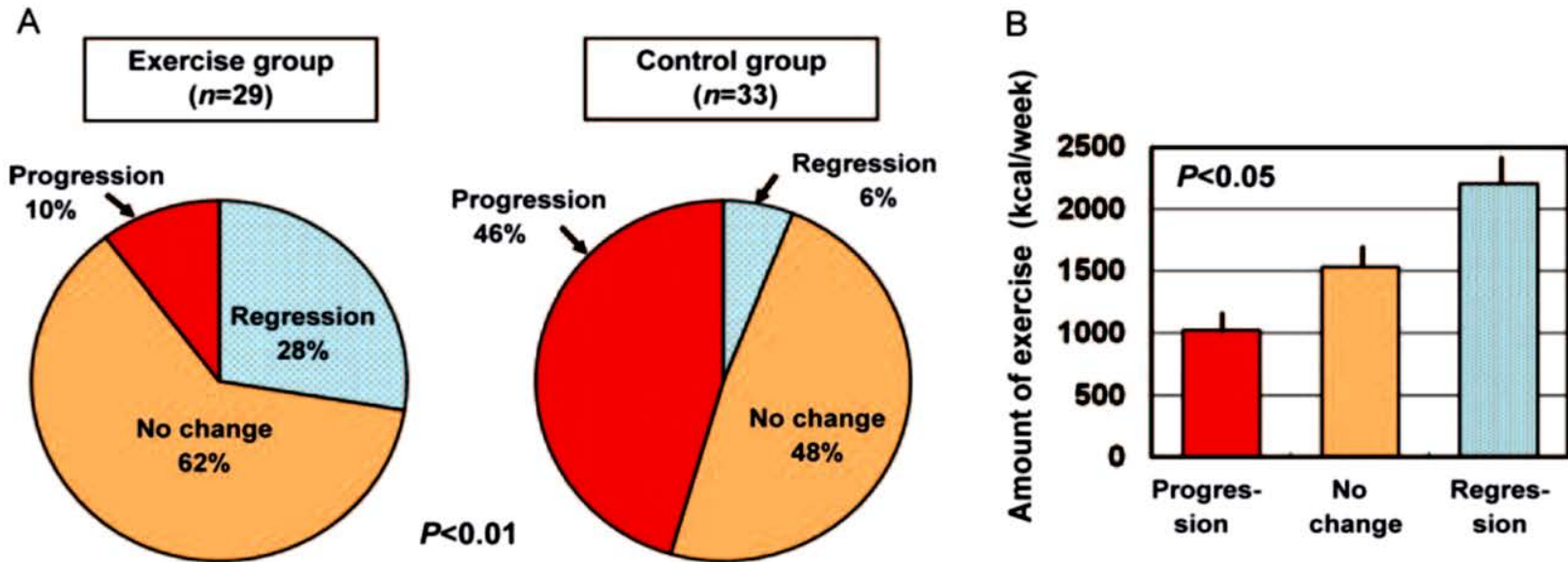


# Exercise Training vs. PCI



Rainer Hambrecht et al. *Circulation*. 2004;109:1371-1378

# Effect of Exercise on Coronary Artery Disease Progression



**Figure 1** (A) Attenuation of progression of coronary atherosclerotic lesions by 12-month exercise training/physical activity in patients with coronary artery disease. (B) The relation between amount of exercise (expressed by energy expenditure) and changes in coronary lesions. Higher levels of exercise training/physical activity were associated with a halt of progression, or even regression, of coronary lesions. (Constructed according to data in Suaya et al.<sup>30</sup>)

# Benefits of Physical Activity on Coronary Risk Factors

- Improved blood lipids
  - ↑ HDL-cholesterol
  - ↓ Triglycerides
  - ↓ Small, dense LDL-cholesterol
- Decreased blood pressure
  - ~ 4/4 mmHg in normotensive subjects
  - ~ 11/6 mmHg in hypertensive subjects
- Improved insulin resistance
- Reduced visceral adiposity
- Reduced hs-CRP

# Comparison of Coronary Arteries in Runners versus Inactive Men

- 11 inactive male volunteers
- 11 male ultradistance runners

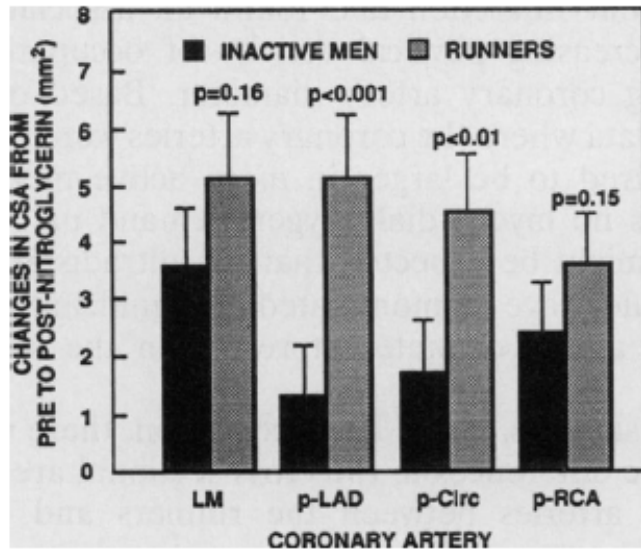
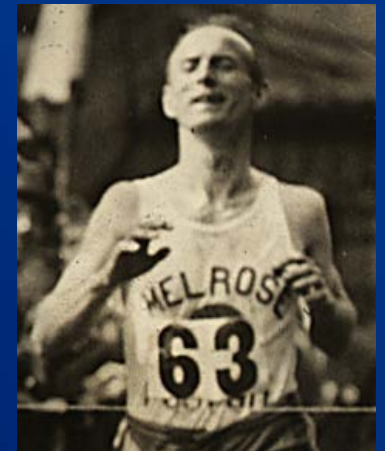


FIGURE 1. Changes between before and after nitroglycerin in the cross-sectional area (CSA) (mm<sup>2</sup>) for the left main (LM) and proximal left anterior descending (p-LAD), circumflex (p-Circ), and right (p-RCA) coronary arteries in physically inactive men and ultradistance runners.

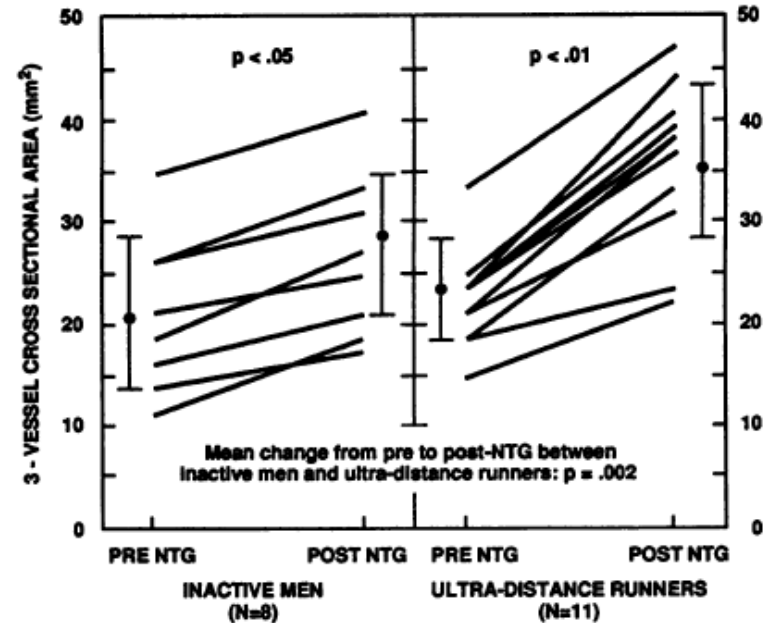
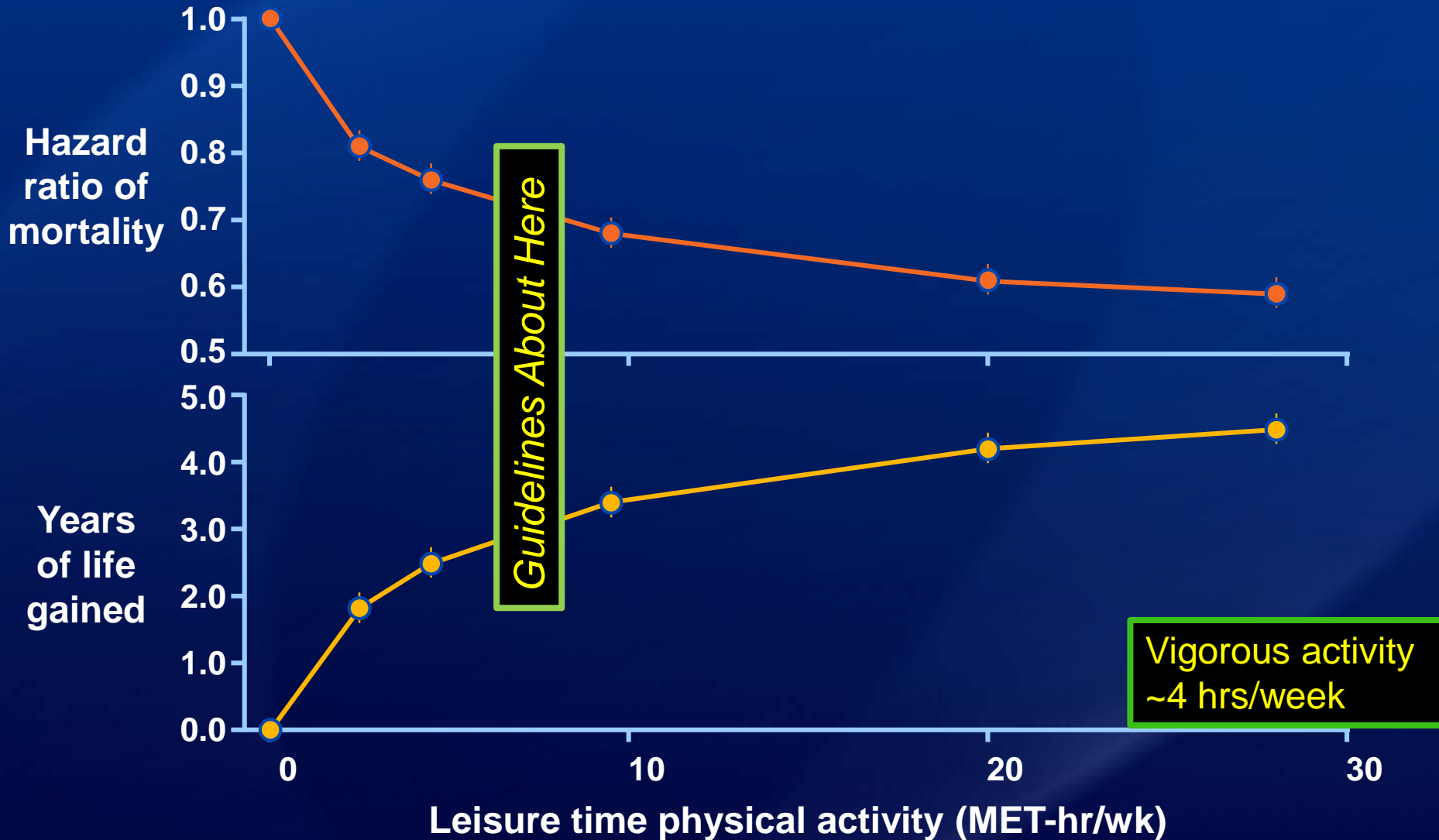


FIGURE 2. Combined cross-sectional area (CSA) (mm<sup>2</sup>) of the proximal right, left anterior descending, and circumflex coronary arteries before and after nitroglycerin for physically inactive men and ultradistance runners.

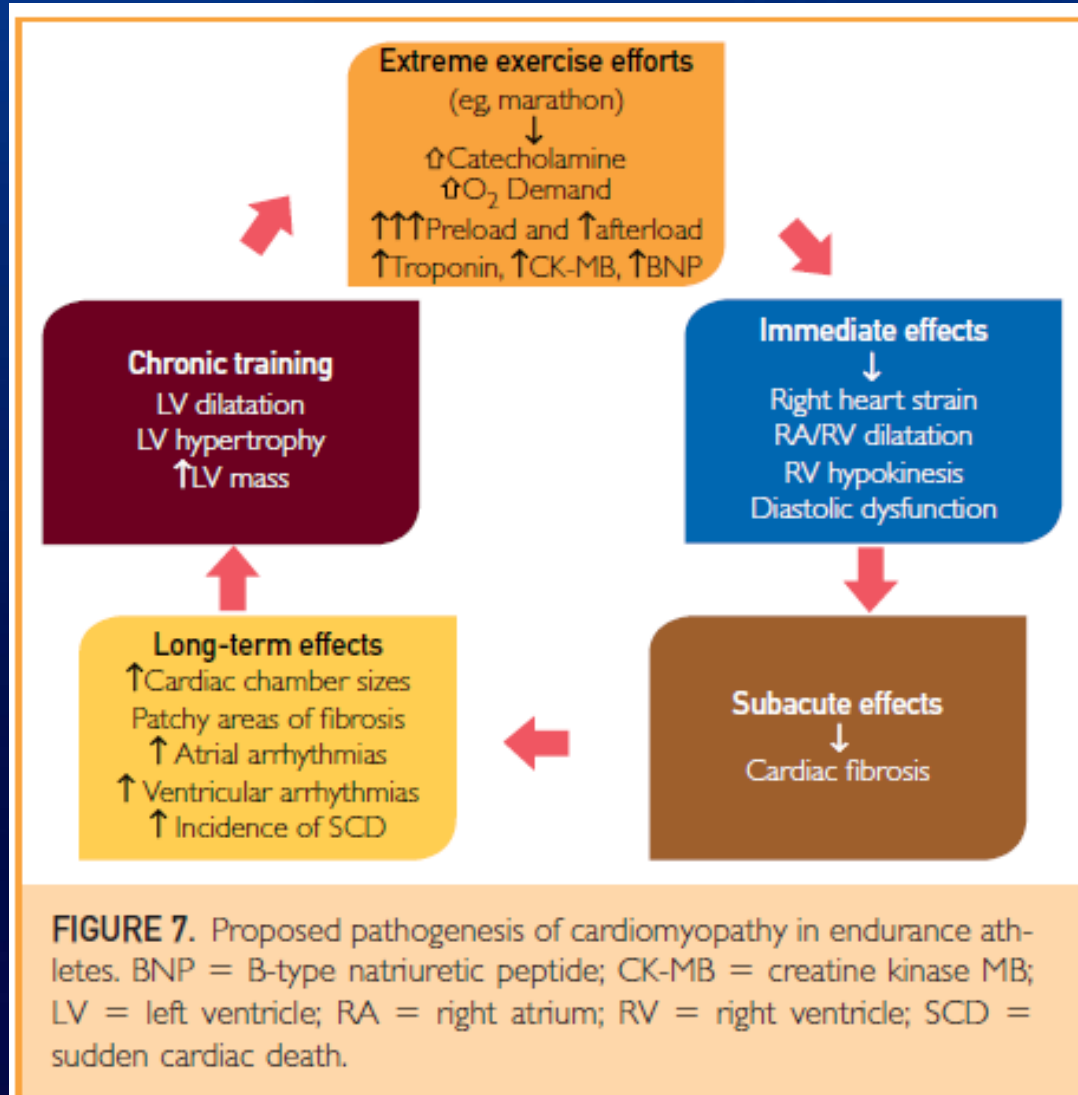
# Physical Activity, Mortality & Longevity

650,000 Adults (Swedes & US, >40 yo)



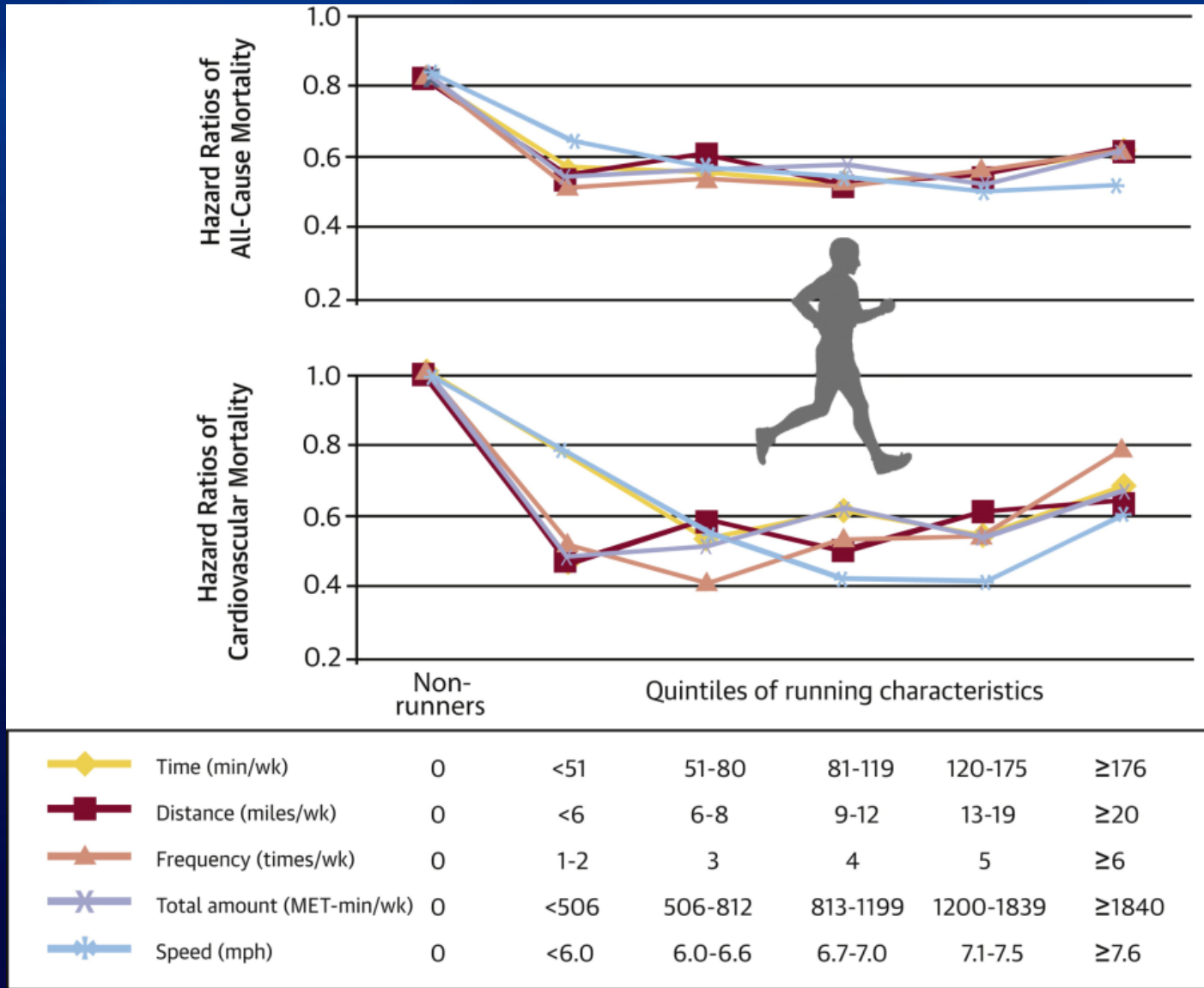
“Is it possible to have  
too much of a good  
thing?”

# Potential adverse cardiovascular effects from excessive endurance exercise



# Leisure-Time Running Reduces All-Cause & CV Mortality Risk

55,137 adults, 18 -100 years of age (mean age 44)



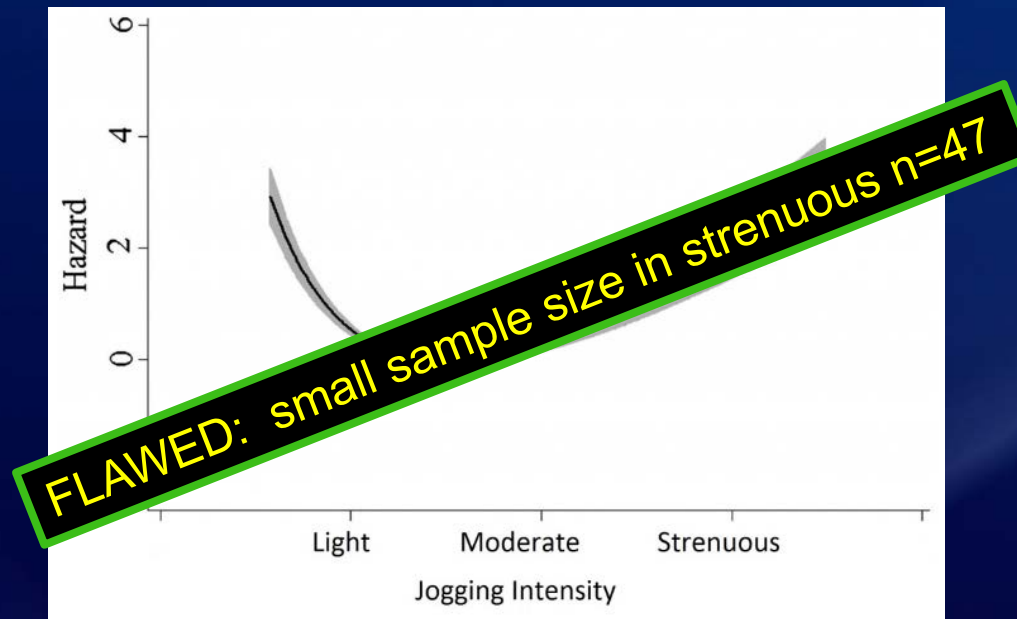


# Dose of Jogging and Long-Term Mortality

## The Copenhagen City Heart Study

1,098 healthy joggers | 3,950 healthy nonjoggers prospectively followed since 2001

- Light joggers – HR = 0.22; 95% CI = 0.10 to 0.47
- Moderate joggers – HR = 0.66; 95% CI = 0.32 to 1.38
- Strenuous joggers – **HR = 1.97; 95% CI = 0.48 to 8.14**

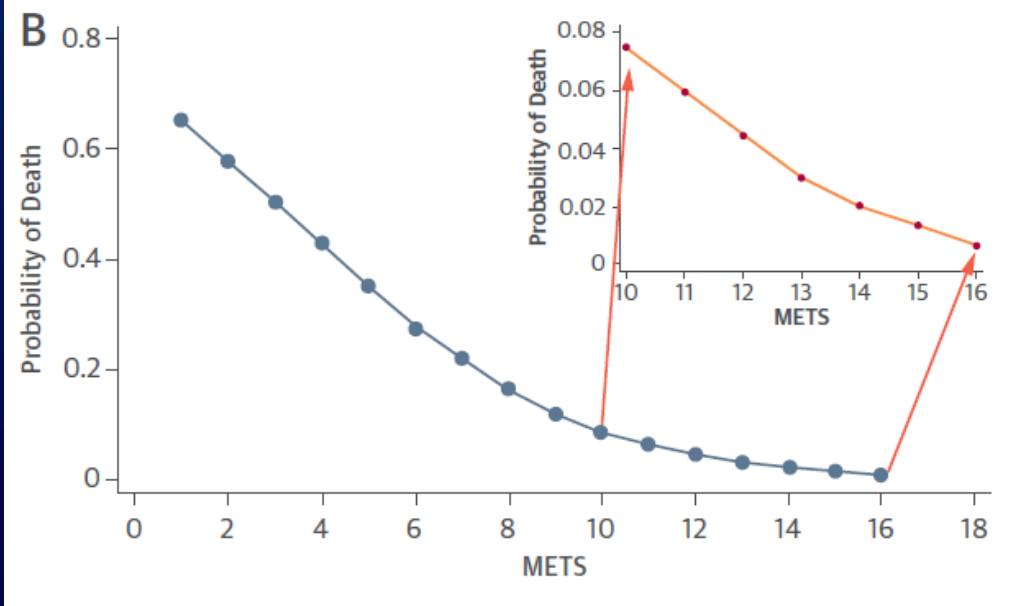
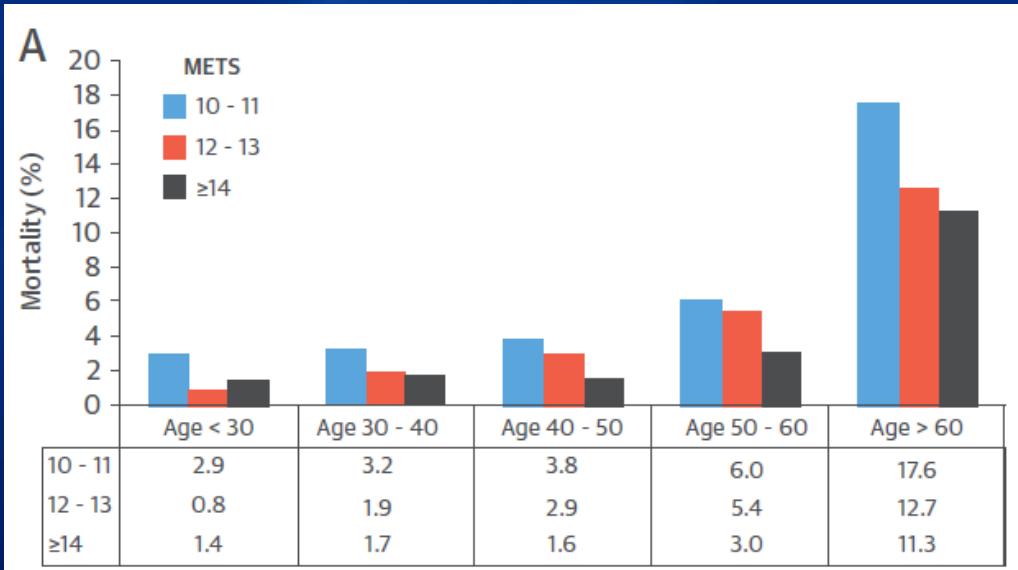


# Too Much Exercise?

The FIT study, Detroit  
 N= 37,855. no CVD, high fitness  
 Mean age 50, 2/3 males

No upper threshold for mortality benefit w/ increasing fitness, even in the most highly fit subjects

“Our data caution against any public health message that might dissuade patients from routine vigorous physical activity with the goal of reaching the highest levels of cardiorespiratory fitness”



# Physical activity in Extreme Environments

Let's move! \_\_\_\_\_



Microgravity wreaks havoc on the body. Astronauts in space work out 2 hours per day to keep their bones and muscles strong.

**heart & vascular system**

#LifeInOrbit



00

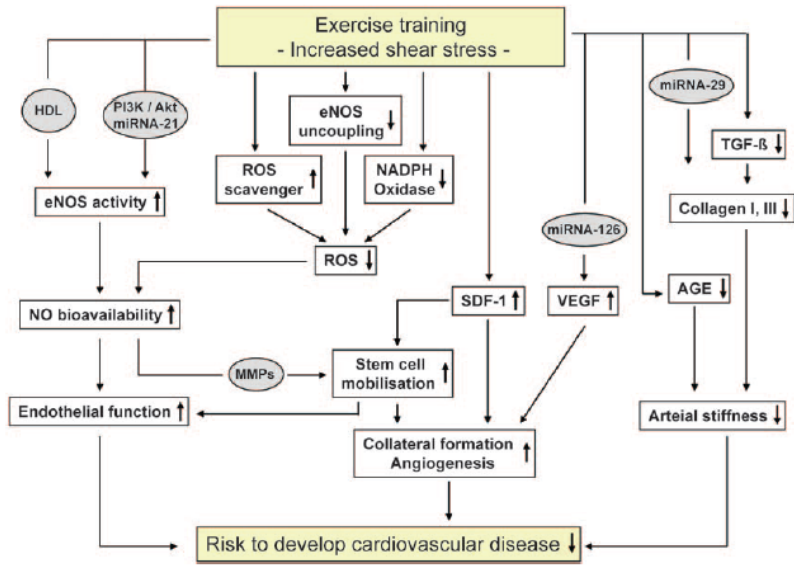
197

196

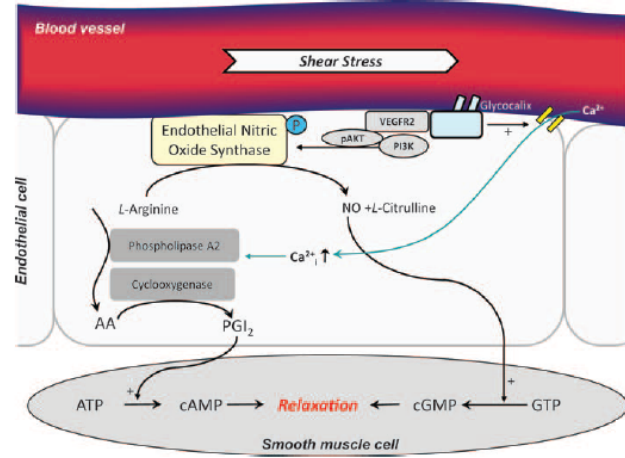
102

# Molecular Mechanisms of Exercise Training

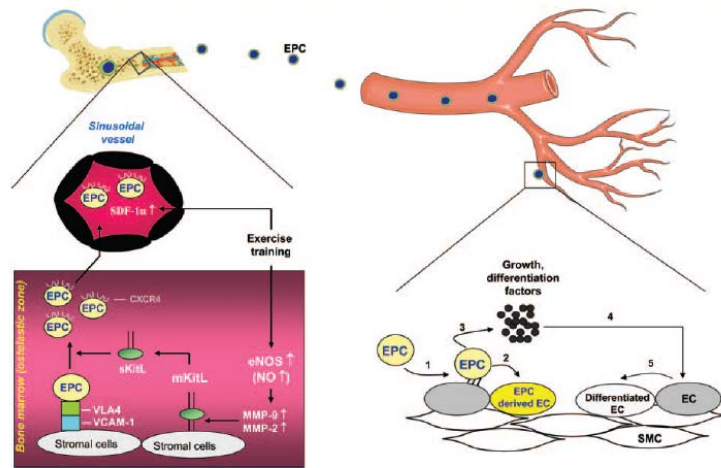
- Endothelial function and NO availability
- Endothelial repair by stem cells
- Reduced arterial stiffness
- Increased production of microRNA
- Collateral growth



**Figure 2** Possible signalling pathways how the beneficial effects of exercise training are translated into a reduced risk of developing vascular disease.



**Figure 3** The majority of exercise effects on the vascular endothelium are mediated by intermittent increases of laminar shear stress. On the luminal side of the endothelial cells, direct signalling can occur through deformation of the glycocalyx activating phospholipase activity via an increase in intracellular  $Ca^{2+}$ , prostaglandin  $I_2$  (PGI<sub>2</sub>) release, and cAMP-mediated smooth-muscle-cell relaxation. VEGF receptor 2 (VEGFR2) can activate PI3K to phosphorylate Akt and induce AKT-mediated eNOS phosphorylation, leading to higher NO production. Akt indicates protein kinase B; AA, arachidonic acid; VEGF, vascular endothelial growth factor.



**Figure 4** Exercise-induced mobilization of EPCs from the bone marrow leading to arteriogenesis or endothelial cell repair. Exercise-induced activation of eNOS and subsequently of MMP-2/9 results in the release of soluble cKit-ligand (sKitL). sKitL confers signals enhancing mobility of EPCs. Along an SDF-1 gradient, the EPCs are mobilized into the peripheral circulation. Once mobilized, the EPCs follow a gradient of SDF-1 or other factor to the site needed, where they bind to mature endothelial cells (EC) via specific cell-surface marker (1). After binding to EC, the EPC may have to find possible pathways to repair the damage in the endothelial cell layer. First, it fills in the gap and differentiates into a mature endothelial cell (2) or secondly it secretes growth differentiation factors (3) which in turn stimulate mature endothelial cells (4) to proliferate and thereby closing the gap in the endothelial cell layer (5). EPC, endothelial progenitor cells.

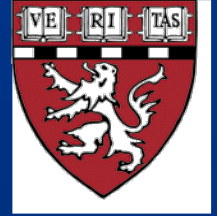
# “The Athlete’s Heart”

P Douglas, 1999

- Increased heart chamber sizes
- Thicker heart muscle
- Improved relaxation of heart
- “sucker heart”
- Slow heart rate



# Cardiac Structural Adaptation to Intensive Training



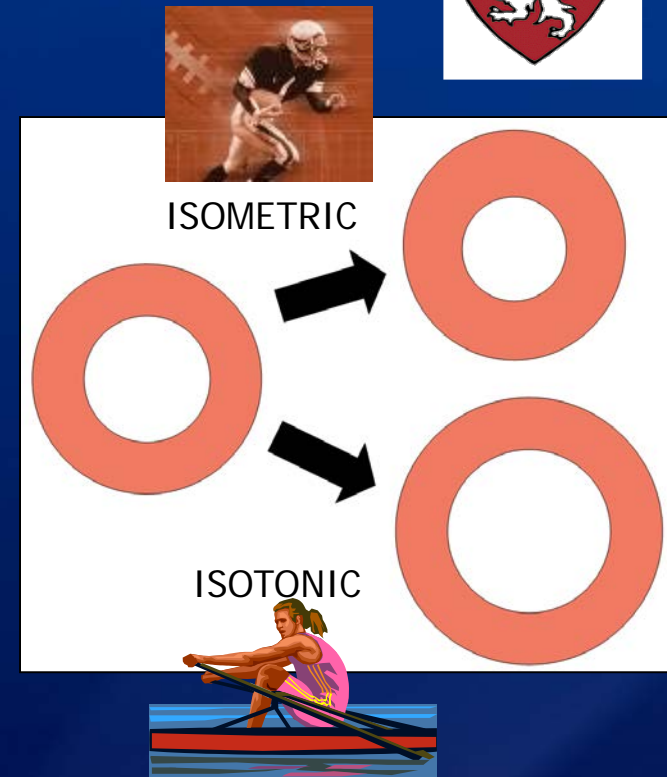
- Hypertrophy

- Eccentric
- Concentric
- Balanced

- Changes in cardiac dimensions:

→ ↑ RA/LA/LV dimensions

→ ↑ Diastolic function: “sucker” vs. “pusher” heart



Baggish A, J Applied Physiology 2008

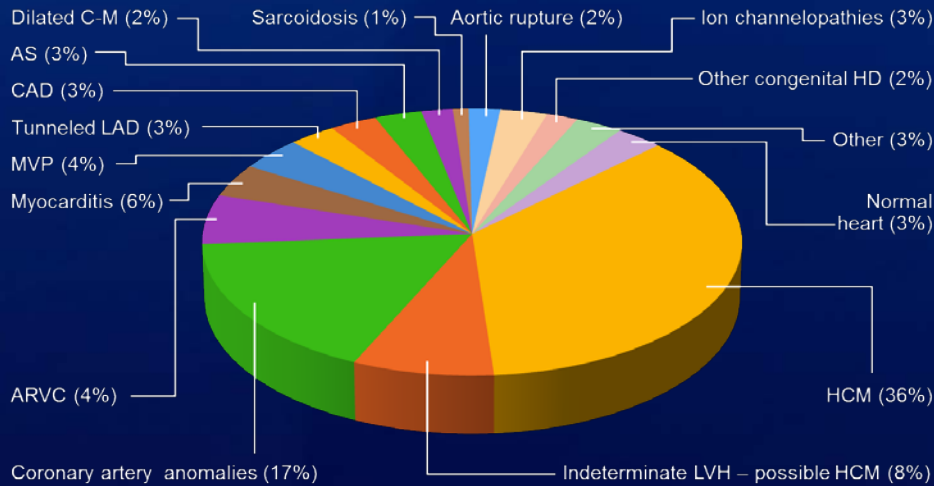
Pluim et al. *Circulation* 1999

Barbier J et al. *Eur J of Cardiovascular Prevention and Rehabilitation* 2006

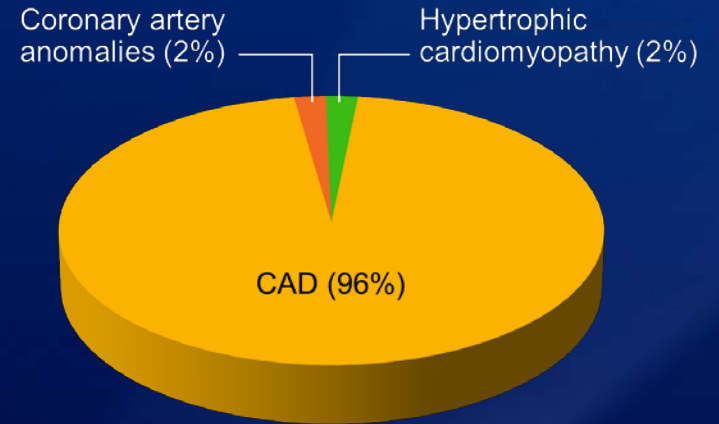


# CV Causes of Sudden Death

## 1,435 Young Competitive Athletes



## Older (Ages 31-65) Athletes



Maron BJ: Circulation 2007;115:1643

Waller: Exercise and the Heart, 1985



# EXTREME PHYSICAL ACTIVITY

## The Marathon

Pheidippides: Marathon -> Athens 490BC



# Marathon Running Physiology

- Unique blend of intensity and duration
  - Fast enough pace to require high VO<sub>2</sub>max
    - < 5:00/mile in elite men; < 5:30/mile in elite women
  - Long enough to cause problems with substrate availability
- Confounding problems
  - Heat transfer and hydration in warm conditions
    - Anything above 55°F

# Effects of Marathon Running on the Heart of “non-elite” athletes

MJ Wood 2006

- Boston Marathon 2004-5 (30/yr)
- Portable echos
- Blood tests
- Population Characteristics
  - 41 males, 19 females
  - Mean age: 41 years (21-65 years)
  - Mean training mileage:  $42 \pm 9$  mi/wk
  - avg finish time: 4hr 5 mins (range 2 hr 55mins to 5hr 55mins)

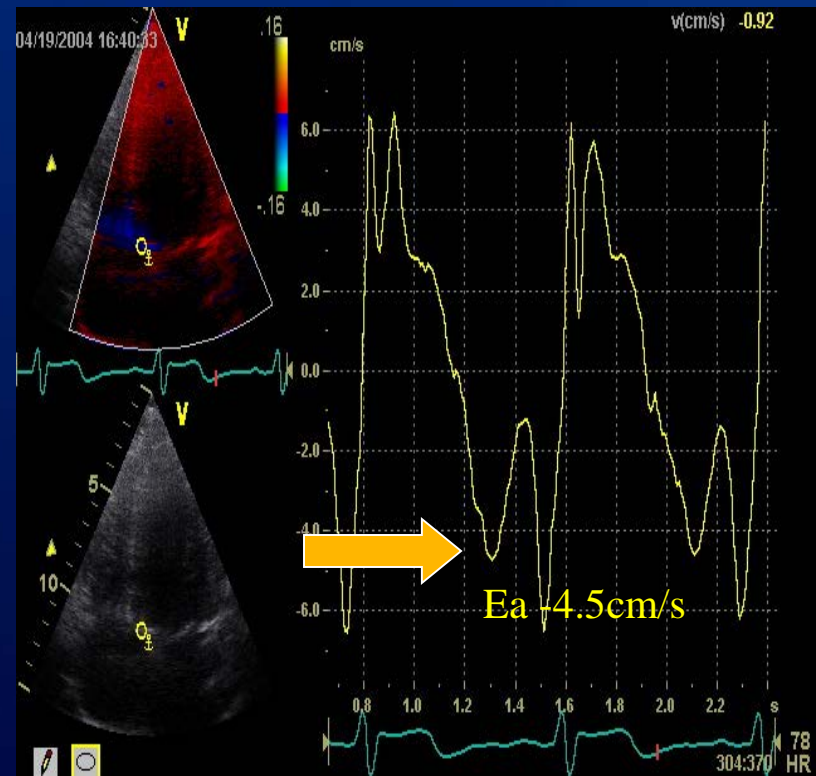
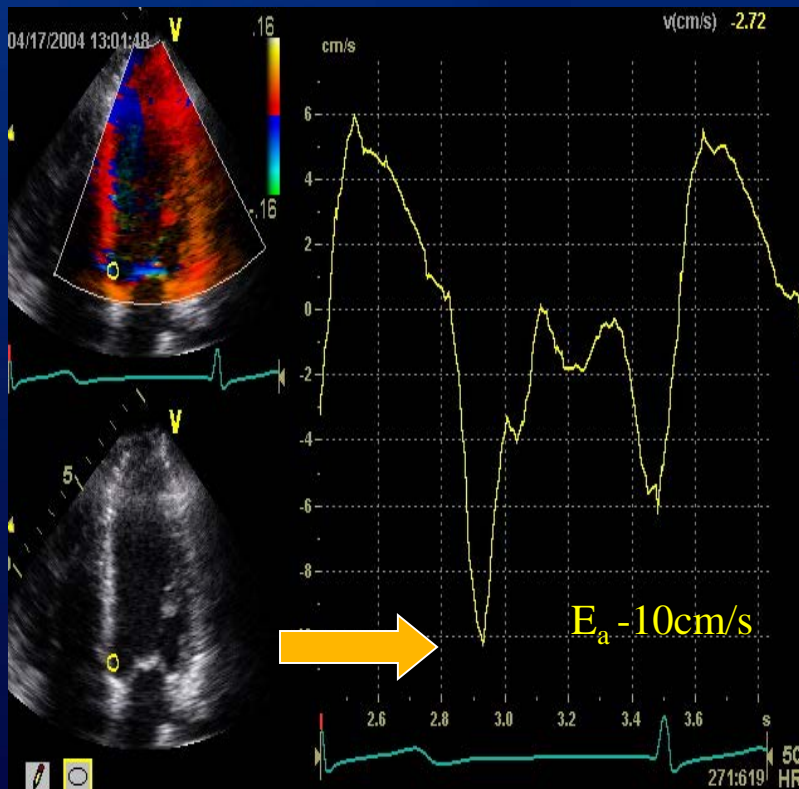
# Effects of Marathon Running on the Heart of “non-elite” athletes

MJ Wood 2006

- Transient alterations in systolic and diastolic function right > left ventricle
- Elevation of cardiac biomarkers
  - used to diagnose MI, CHF
- **These findings were directly associated with training mileage: <35-40 miles/wk**

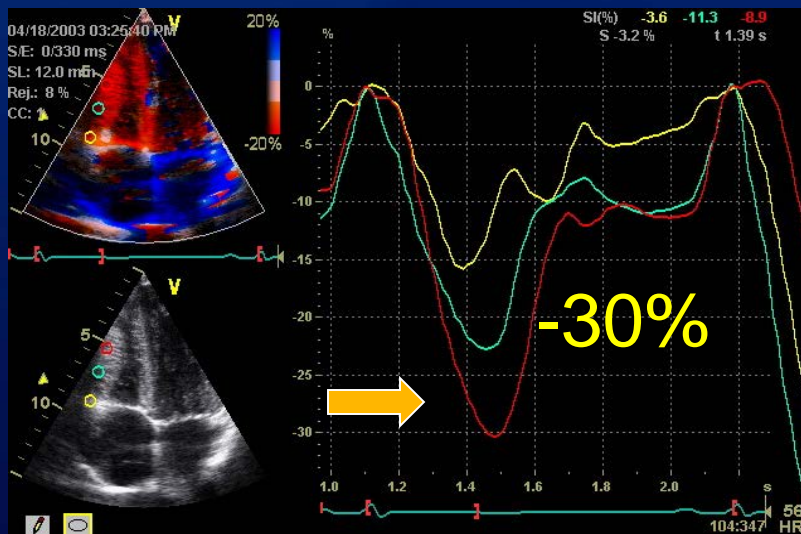
# 42 y/o male runner

## Tissue Doppler Pre and Post Marathon (3:28 marathon)

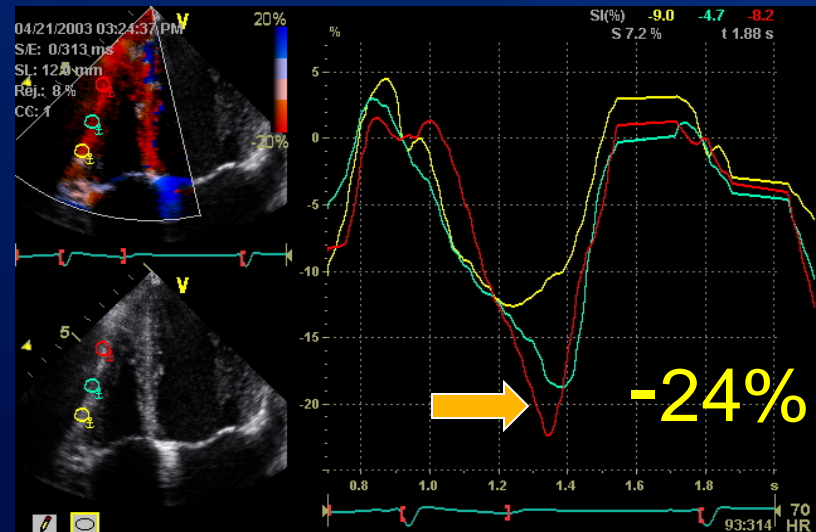


# RV Strain

Pre-marathon  
RV free wall  $\epsilon$



Post-marathon  
RV free wall  $\epsilon$



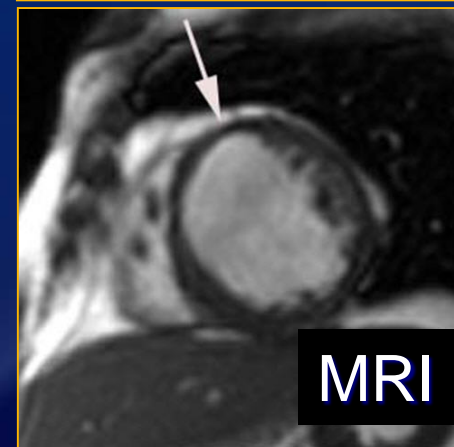
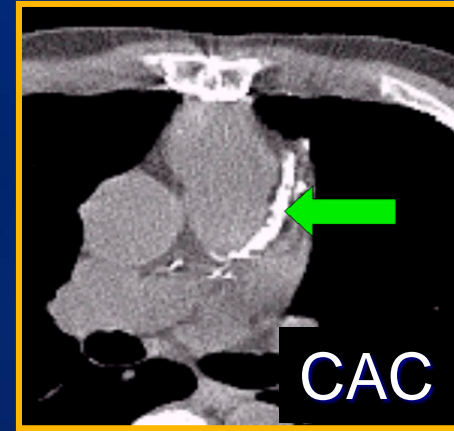


# Running: the Risk of Coronary Events

## Prevalence and prognostic relevance of CAD in marathon runners

Essen Marathon Study, Germany: Eur Heart J, April 2008

- 108 “healthy” male runners >50 yo
  - >5 marathons in 3 yrs
- Methods: FRS, CAC, MRI
- Conclusions:
  - Fram Risk score underestimated CAC
  - Higher CAC with more marathons
  - As CAC ↑ so did “heart scar” on MRI
- Limitations: -no women
  - selection bias: pre-existing disease?



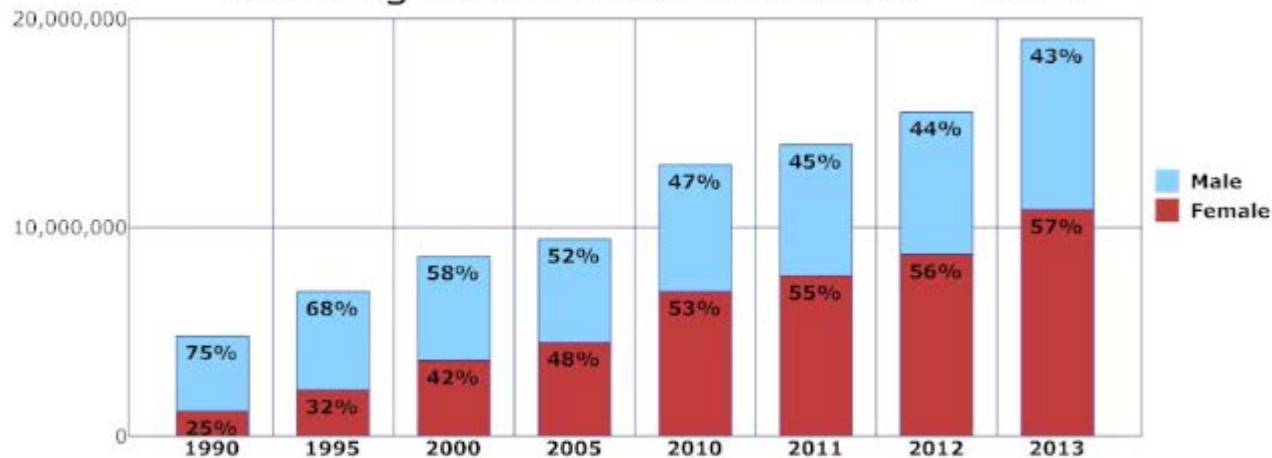


## Incidence of SCA

- 5.4 per million marathon participants
- 18.6 per million per NCAAathlete/yr

54% > 35 years old  
57% female

Running Event Finishers 1990 - 2013



	1990	1995	2000	2005	2010	2011	2012	2013
Female	1,199,200	2,215,500	3,619,600	4,494,400	6,929,000	7,685,700	8,699,000	10,844,200
Male	3,597,800	4,708,000	4,998,400	4,947,600	6,071,000	6,288,300	6,835,000	8,180,800

<http://www.runningusa.org/2014-state-of-the-sport-part-III-us-race-trends>  
accessed 10-19-2015



Thursday, October 8, 2015 - 1:27 p.m.

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# Mayo Clinic News Center

Mayo Clinic

September 29th, 2015 · [Leave a Comment](#)

## Saving a Life While Barely Breaking Stride

By *intheloop*



**Sports-related SCA is more likely to be a witnessed event, suffer ventricular fibrillation, receive timely CPR and have higher survival to hospital discharge**

Marijon E,  
Circulation.  
2015;131:1384-91

Bystander CPR and use of AED for rapid cardiac defibrillation --strongest independent predictors for survival to hospital discharge among sports-related SCA patients-hands only CPR – mass training pre-marathon events

# Sports Paradox

- vigorous activity (>6 METs) acutely and transiently increases the risk of SCA and AMI (~5X)
- regular habitual exercise mitigates that risk
- relative risk of SCA and exercise:
  - inversely related to habitual exercise level
  - ~50 X higher in sedentary
  - ~40% lower among men with highest level of habitual vigorous activity

Mittleman MA *N Engl J Med.* 1993;329:1677-83

Albert CM *N Engl J Med.* 2000;343:1355-61

Siscovick DS, *N Engl J Med.* 1984;311:874-7

# Sudden Cardiac Arrest (SCA) During Sports Activity

- Overwhelmingly, the majority of sports-related SCAs have occurred in **men (HR 18X)**
- Potential explanations include:
  - historically lower participation rates for women in events
  - women tend to develop atherosclerosis ~10 yrs later than men
  - gender differences
    - atherosclerotic plaque morphology
    - ventricular electrical activity
    - autonomic factors

# What is the effective dose of exercise?



# Physical Activity Recommendations: Given the extensive CV benefits of exercise

- $\geq 150$  min/wk of moderate, or 75 min/wk of vigorous exercise training (or an equivalent combination of both)
- Minimum 30 min of moderate-intensity physical activity (continuous or in 10-minute increments), preferably most days of week
- Equivalent to ~1.5 miles/day of brisk walking
- Even 15 min/day or 90 min/wk is associated with a survival benefit compared with physical inactivity

Haskell WL, Circulation. 2007;116(9):1081-1093

Fletcher GF, Circulation. 2013;128:8

Global Recommendations on Physical Activity for Health. World Health Organization. Available at: [http://www.who.int/dietphysicalactivity/factsheet\\_recommendations/en/](http://www.who.int/dietphysicalactivity/factsheet_recommendations/en/).

Physical Activity Guidelines for Americans. U.S. Department of Health and Human Services. Available at: <http://health.gov/paguidelines>

# Recommendations for your patient

- Assess the potential impact of increased physical activity for the individual patient
- Start with a level of exercise appropriate to the baseline fitness and activity level of the patient
- Progressively advance the exercise prescription until risk factors are optimally controlled ... or limits of tolerance are reached



# Implications of Recent Trials

- High intensity interval training more effective than continuous low-moderate intensity training
- Supervised training superior to home programs
  - Both HF-ACTION and LOOK AHEAD had more frequent supervised sessions initially, tapering off to home program as study progressed

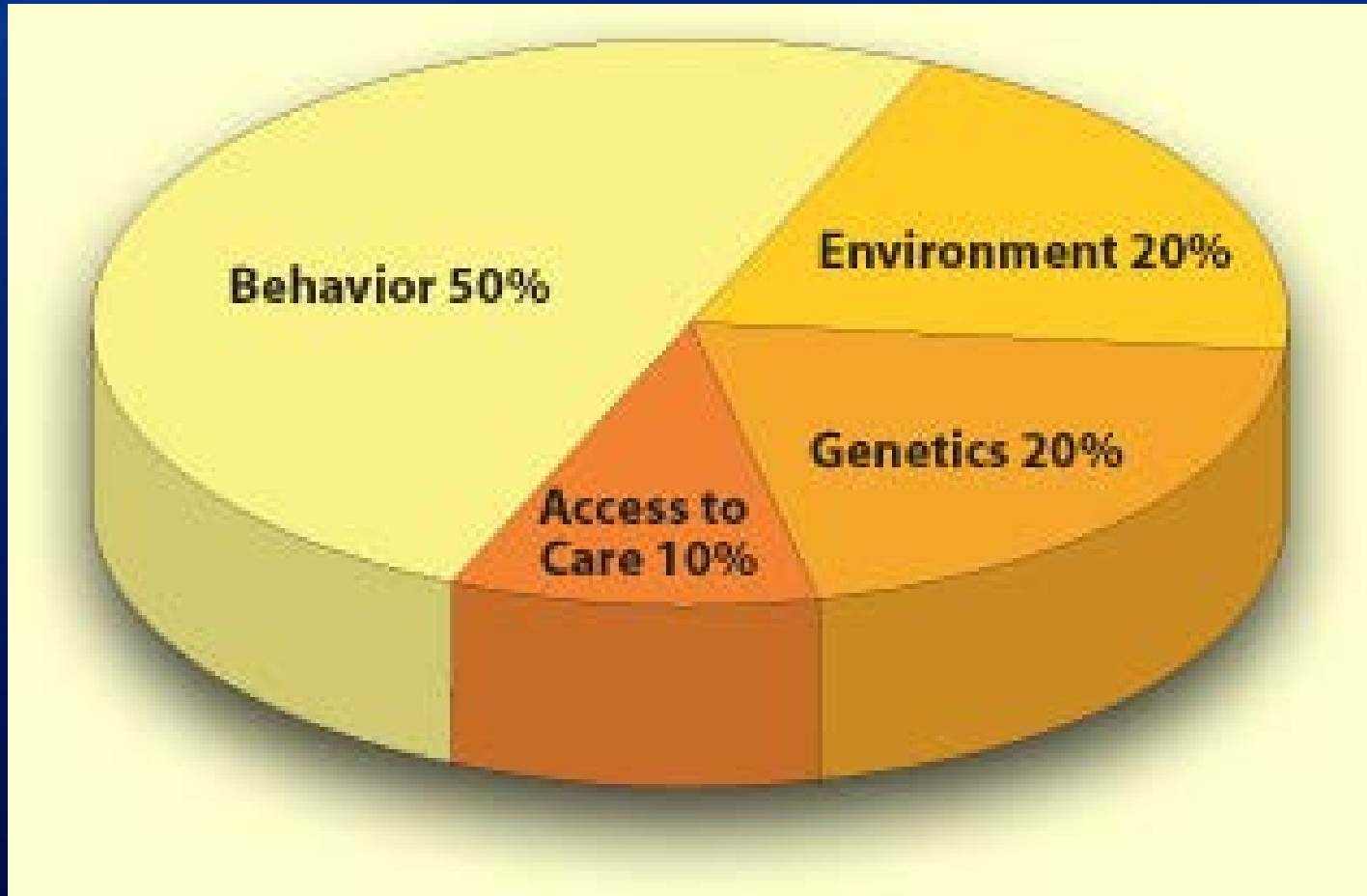
Exercise is great medicine,  
but sometimes it can be a hard pill to swallow



Explains negative results in LOOK AHEAD and HF-ACTION

## ***COMPLIANCE ISSUES***

# Determinants of Health



# Behavior Changes When Observed

## Personal Activity Monitors – Many Types



# Incorporating Physical Activity into your workday: “The Active Office”

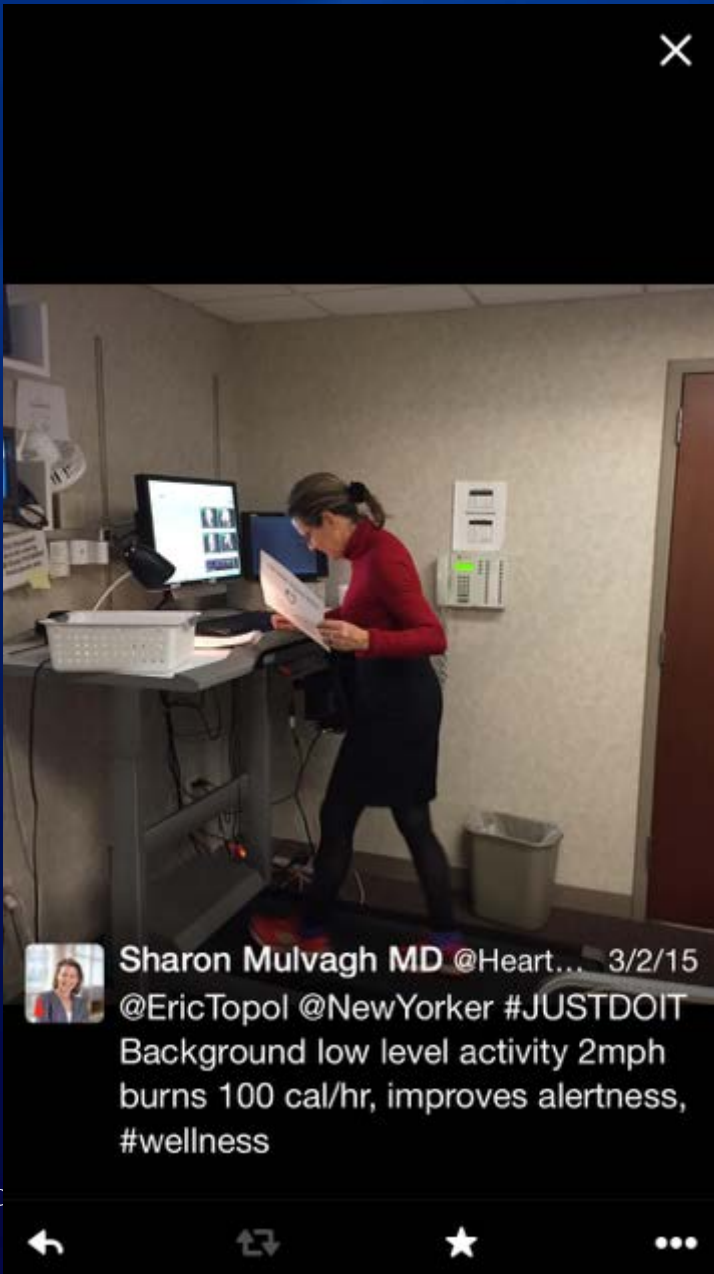


Workout  
while  
you  
work!

*Dr. James Levine & Walking Workstation*

# MAYO ECHOLAB

# MSP AIRPORT



STATE-OF-THE-ART PAPERS

## Sports and Exercise Cardiology in the United States

### Cardiovascular Specialists as Members of the Athlete Healthcare Team

Christine E. Lawless, MD,\*† Brian Olshansky, MD,‡ Reginald L. Washington, MD,§  
Aaron L. Baggish, MD,|| Curt J. Daniels, MD,¶ Silvana M. Lawrence, MD, PhD,#  
Renee M. Sullivan, MD,\*\* Richard J. Kovacs, MD,†† Alfred A. Bove, MD, PhD‡‡

Chicago, Illinois; Lincoln, Nebraska; Iowa City, Iowa; Denver, Colorado; Boston, Massachusetts;  
Columbus, Ohio; Houston, Texas; Columbia, Missouri; Indianapolis, Indiana; and Philadelphia, Pennsylvania



In recent years, athletic participation has more than doubled in all major demographic groups, while simultaneously, children and adults with established heart disease desire participation in sports and exercise. Despite conferring favorable long-term effects on well-being and survival, exercise can be associated with risk of adverse events in the short term. Complex individual cardiovascular (CV) demands and adaptations imposed by exercise present distinct challenges to the cardiologist asked to evaluate athletes. Here, we describe the evolution of sports and exercise cardiology as a unique discipline within the continuum of CV specialties, provide the rationale for tailoring of CV care to athletes and exercising individuals, define the role of the CV specialist within the athlete care team, and lay the foundation for the development of Sports and Exercise Cardiology in the United States. In 2011, the American College of Cardiology launched the Section of Sports and Exercise Cardiology. Membership has grown from 150 to over 4,000 members in just 2 short years, indicating marked interest from the CV community to advance the integration of sports and exercise cardiology into mainstream CV care. Although the current athlete CV care model has distinct limitations, here, we have outlined a new paradigm of care for the American athlete and exercising individual. By practicing and promoting this new paradigm, we believe we will enhance the CV care of athletes of all ages, and serve the greater athletic community and our nation as a whole, by allowing safest participation in sports and physical activity for all individuals who seek this lifestyle. (*J Am Coll Cardiol* 2014;63:1461-72) © 2014 by the American College of Cardiology Foundation

Confirmation of the benefits of exercise (1-4), increased participation in organized athletics, and efforts to combat the obesity epidemic have led to marked increases in the numbers of Americans participating in sports and exercise in all major demographic groups over the last decade (5-9). Among athletes ≤35 years of age, 44 million youth (≤18 years of age) participate annually in organized sports, with 7.7 million and 463,202 engaged at the high school and collegiate levels, respectively (6,7). Older, or master, athletes (≥35 years of age), are particularly drawn to endurance sports. Marathon finishers have increased from 353,000 in

2000 to over 500,000 in 2011 (8); U.S. triathlon memberships have increased from 21,341 to more than 146,000 during the same period (9). Simultaneously, as children and adults with established heart disease are living longer with improved quality of life, many have contemplated participation in sports and exercise (10).

Paradoxically, despite its favorable effects on well-being and survival, exercise can acutely increase the risk of myocardial infarction (11,12), aortic dissection (13,14), arrhythmias (15-19), and sudden cardiac arrest (SCA) (Online Appendix) and/or death (SCD) (20,21). Chronically,

and Desai Medical, has served as a speaker for Medtronic, and has received honoraria from Boston Scientific, Medtronic, Daiichi Sankyo, Boehringer Ingelheim, BioControl, Amarin, and Sanofi-Aventis. Dr. Daniels receives financial support for research from Actelion, United Therapeutics, Glaxo, Bayer, Amplatzer, and the National Institutes of Health. Dr. Sullivan receives financial support from Biogen for the EPIC Alliance. Dr. Bove has served as a consultant to Insight Telehealth Systems, LLC, and World Health Networks, Inc., and has stock ownership in Insight Telehealth Systems, LLC. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received November 12, 2013; revised manuscript received December 17, 2013; accepted December 24, 2013.

From the \*University of Chicago and Sports Cardiology Consultants LLC, Chicago, Illinois; †Bryan Heart—University of Nebraska, Lincoln, Nebraska; ‡University of Iowa Hospitals, Iowa City, Iowa; §Rocky Mountain Hospital for Children, Denver, Colorado; ||Harvard University and Massachusetts General Hospital, Boston, Massachusetts; ¶The Ohio State University and Nationwide Children's Hospital, Columbus, Ohio; #Baylor College of Medicine and Texas Children's Hospital, Houston, Texas; \*\*University of Missouri, Columbia, Missouri; ††Indiana University School of Medicine, Indianapolis, Indiana; and the ‡Temple University Hospital, Philadelphia, Pennsylvania. Dr. Olshansky has served on the data and safety monitoring boards of Boston Scientific, Amarin, and Sanofi-Aventis; has served as a consultant to Boston Scientific, BioControl, Boehringer Ingelheim, Daiichi Sankyo,

CONFERENCE REPORT

## Protecting the Heart of the American Athlete

Proceedings of the American College of Cardiology Sports and Exercise Cardiology Think Tank  
October 18, 2012, Washington, DC



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The findings and conclusions in this report are those of the conference participants and do not necessarily reflect the official position of the American College of Cardiology.

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Our generic '**Exercise Medicine Label**' transforms how patients prevent and treat many chronic diseases with the help of a format that health professionals see and can recommend as a '**Medicine**'



### Directions for use

At least 30 minutes 5 days a week, or 150mins of exercise a week.

### Side effects

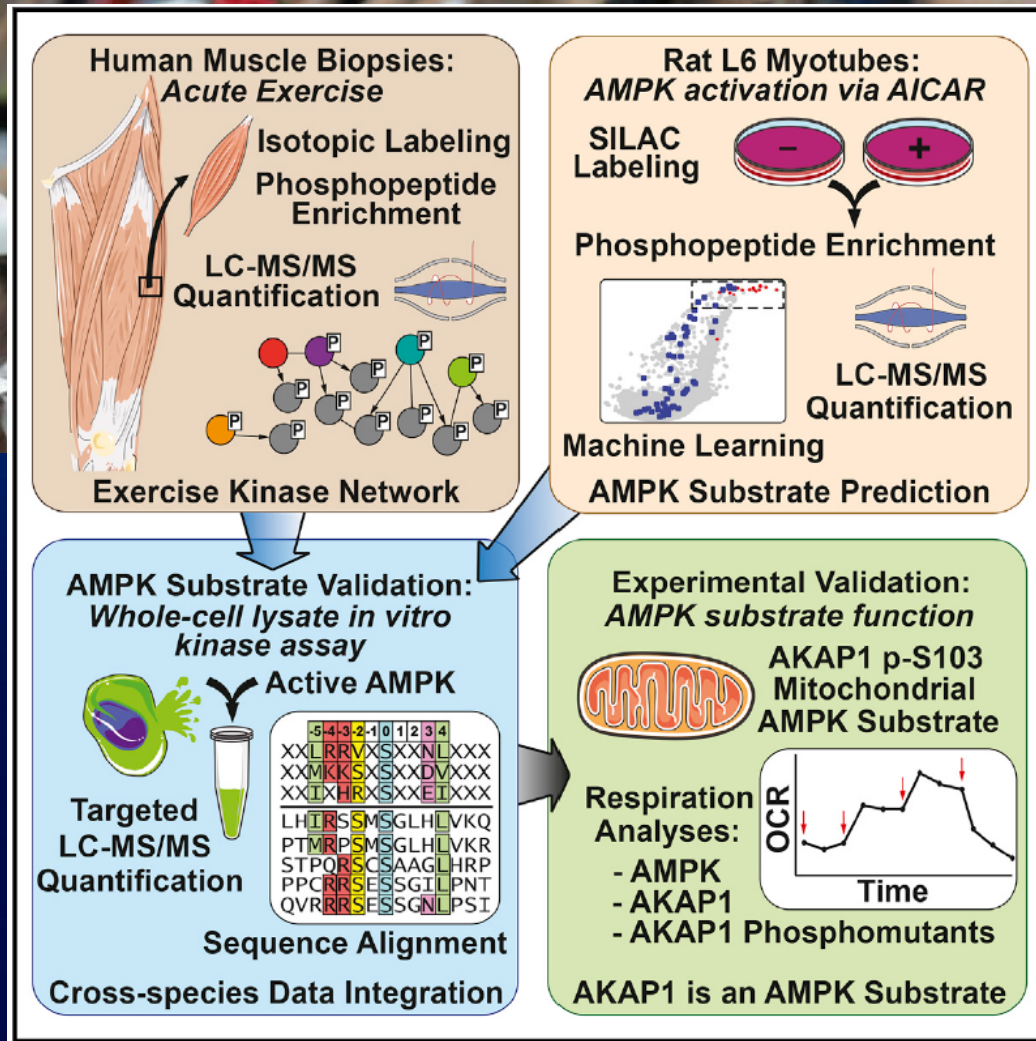
- 35-40% Reduction in risk of heart related events
- 50% reduction in breast cancer death
- 50% reduction in bowel cancer death
- 42% reduction in diabetes related death
- 42% reduction in risk of developing diabetes
- A significant reduction in blood pressure: about 7mmHg systolic and nearly 6mmHg diastolic
- Reduction in risk of falls and maintenance of bone health in men and post menopausal women
- And generally happier, healthier patients!

### Uses

For the prevention and treatment of most non communicable diseases such as: heart disease, cancer, hypertension, stroke, obesity, diabetes, osteoporosis, mental health problems, parkinson's disease, multiple sclerosis, asthma, chronic obstructive airways disease, musculoskeletal problems and for over 100 different diseases that commonly present to family and hospital doctors and a wide variety of allied health professionals.



# Scientists are working on an "exercise pill" so you never have to work out again



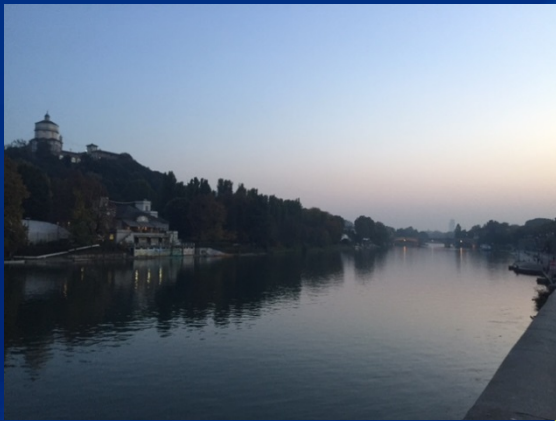
# Summary

## Effects of Physical Activity on the Heart

- Benefits on decreasing CV disease risk; 1<sup>o</sup> & 2<sup>o</sup> prevention
- Controversy regarding “dose of exercise”, potential adverse effects of extreme endurance exercise
- Perspective on SCA during sports activities; rare, but increasing due to increasing participation, predisposing factors; “prevention gap”
- Current physical activity recommendations for heart health
- IT solutions to improving adherence

The long-term benefits outweigh the short-term risks related to physical activity.

"If you survive exercise, which you almost certainly will, you will undoubtedly live longer and healthier"



Gracias! Thank You!

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