



The Dangers of Too Little VS Too Much Exercise



Robert E. Sallis, MD, FAAFP, FACSM

Co-Director,
Sports Medicine Fellowship
Kaiser Permanente; Fontana, CA

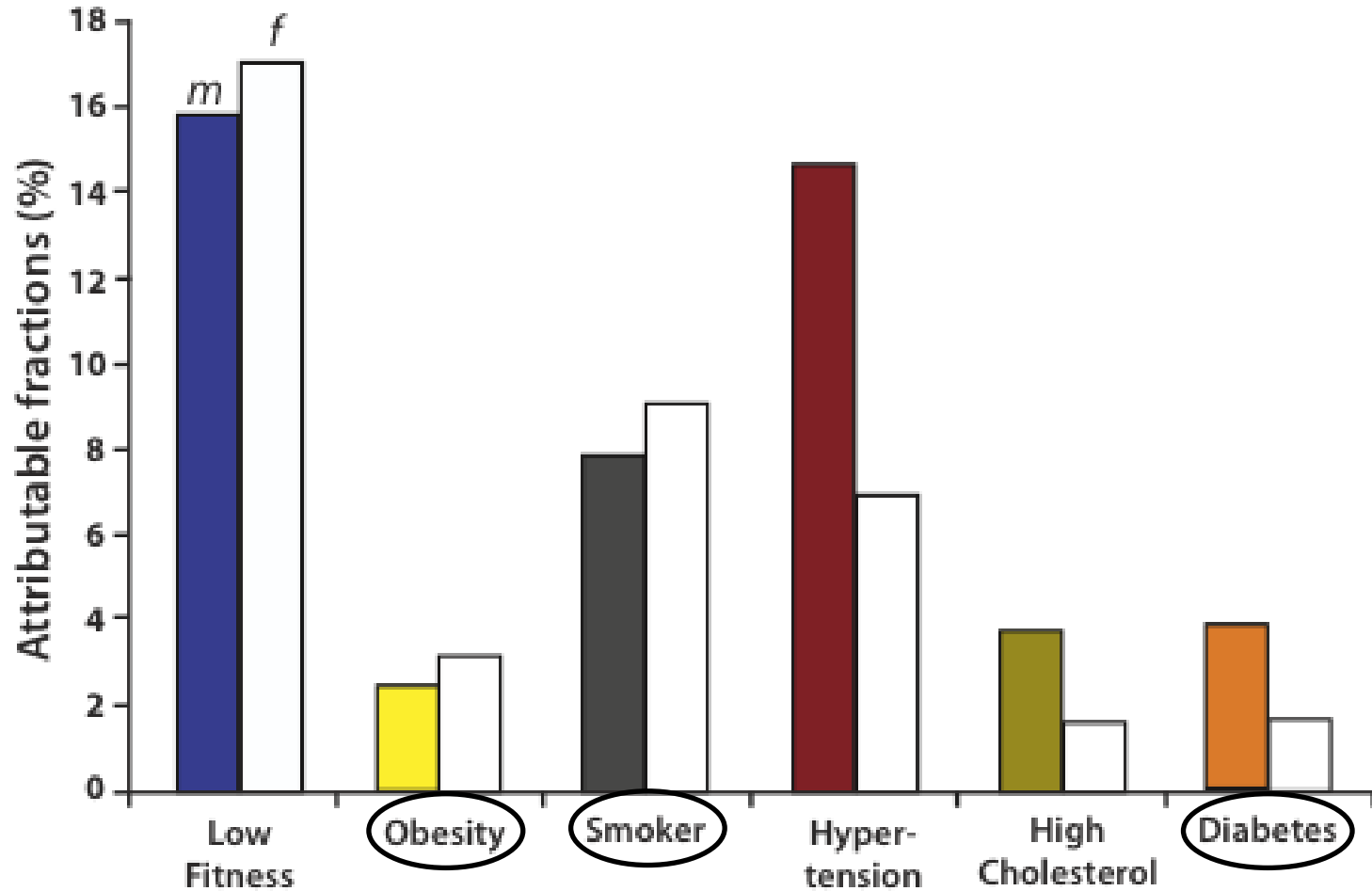
Chair,
Exercise Is Medicine
Advisory Board

Clinical Professor
Family Medicine
UC Riverside
School of Medicine

Exercise and Health

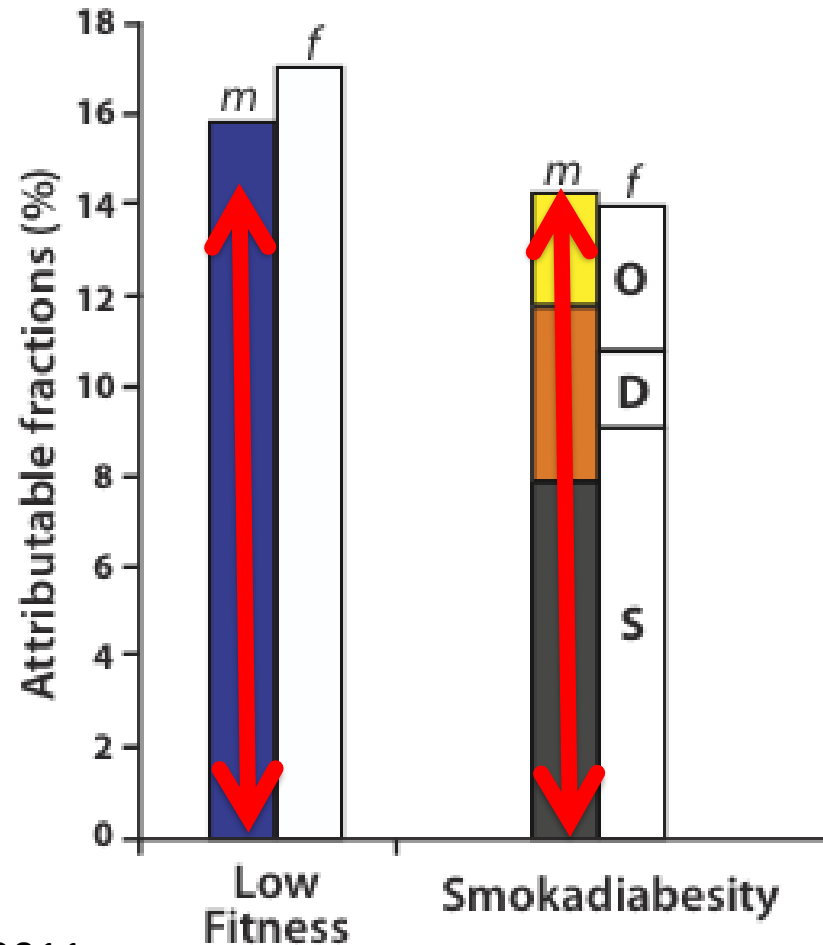
- We know that exercise is a powerful medicine for both the treatment and prevention of chronic disease and reducing the risk for premature death.
 - Proven linear relationship between physical activity and health status.
 - The association between disease and an inactive and unfit way of life persists in every subgroup of the population.
- Too little exercise is THE major public health problem of our time.

Comparing the Danger of *Low Fitness*



Blair; 2008

Low Fitness Kills More *People* than *Smokadiabesity*!



Khan; BJSM, 2011


The Classification of Risk Factors for Cardiovascular Disease

- Surrogate outcomes of poor lifestyle choices and stress (hypertension, obesity, cholesterol and diabetes), along with smoking are given “causal” risk factor status for CVD.
- Physical inactivity is generally referred to as a “predisposing” risk factor.
 - Suggesting its influence on disease is entirely due to intensification of the causal factors.
 - Result has been disproportionate focus on drugs (mainly lipid and BP) to treat disease.
 - Research has proven this is incorrect.

The Effect of Exercise on CVD Risk

- Even after accounting for traditional CVD risk factors (BP, DM, lipids, weight), the inverse relationship between PA & CVD risk persists.
 - ~59% of the reduction in CVD risk with exercise is due to reducing Inflammation & Clotting (32.6%), BP (27.1%), lipids (19.1%), BMI (10.1%), A1C (8.9%).
 - *41% of risk reduction due to other unknown mechanisms* (perhaps endothelium function and remodeling or LV structure and function).
 - Effect of *weight loss* is only on traditional risk factors.

The Effect of Exercise on CVD Risk

- Even after accounting for traditional CVD risk factors (BP, DM, lipids, weight), the inverse relationship between PA & CVD risk persists.
 - ~59% of the reduction in CVD risk with exercise is due to reducing Inflammation & Clotting (32.6%), BP (27.1%), lipids (19.1%), BMI (10.1%), A1C (8.9%).
 - 41% of risk reduction due to other unknown mechanisms (perhaps endothelium function and remodeling or LV structure and function).
 - Effect of *weight loss* is only on traditional risk factors.
- 

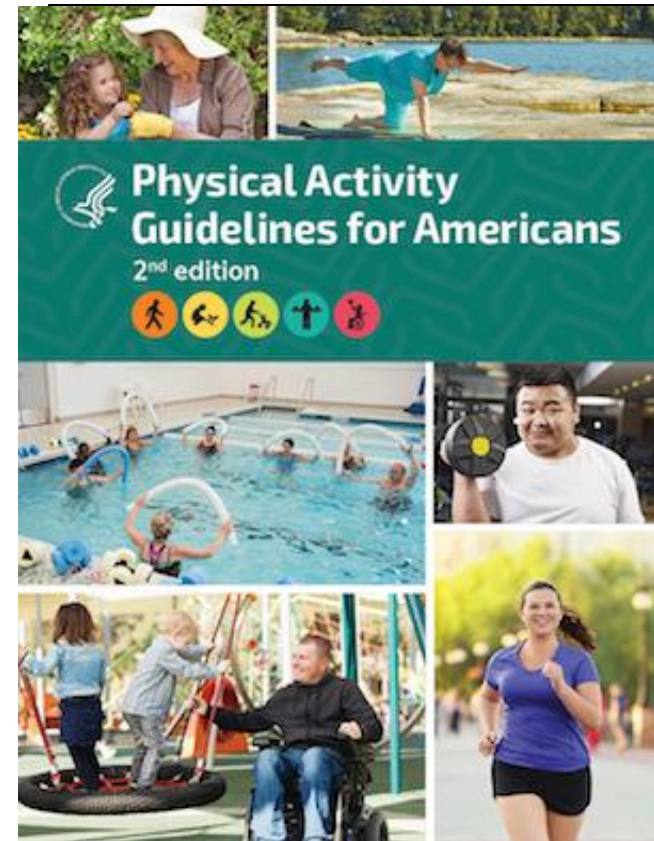
Irrefutable Evidence that Exercise is Medicine for the Primary and Secondary Prevention of:

- Diabetes mellitus
- Cancer (breast and colon)
- Hypertension
- Depression
- Osteoporosis
- Dementia
- Coronary Artery Disease
- Lower death rate from all causes

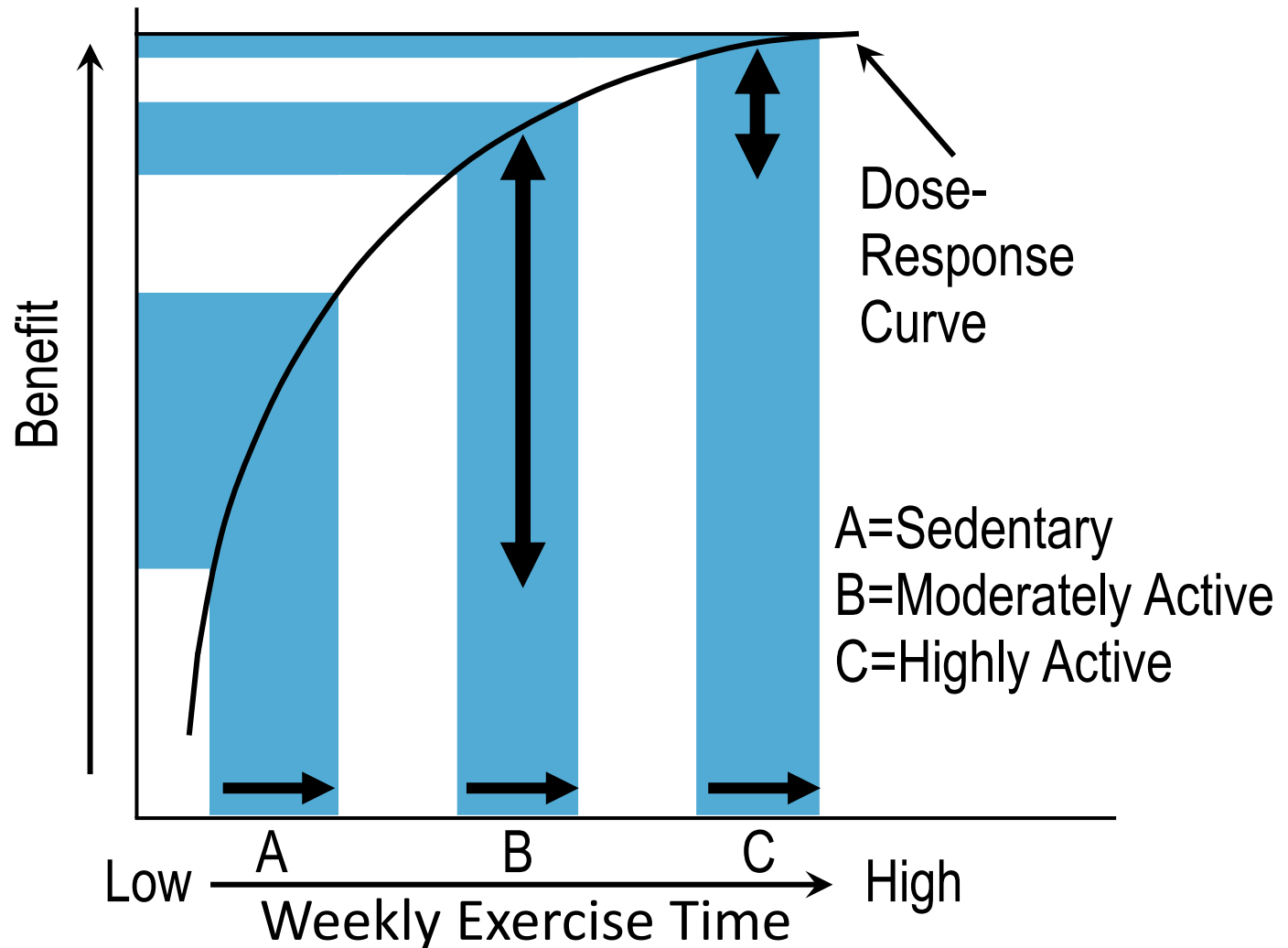
What is the Optimal Dose of Exercise?

2018 US Physical Activity Guidelines

- 150 minutes per week of moderate to vigorous PA (like a brisk walk) in adults.
 - 30 minutes walking on 5 days per week.
 - Activity bouts of any duration count!
- 75 minutes per week of vigorous exercise (like running).
- 60 minutes per day in kids (half at vigorous intensity).



Dose-Response Curve for Exercise



Exercise is Medicine

*Running and Walking are 2 great formulations,
but what is the optimal dose of each?*



Let's Start With Running



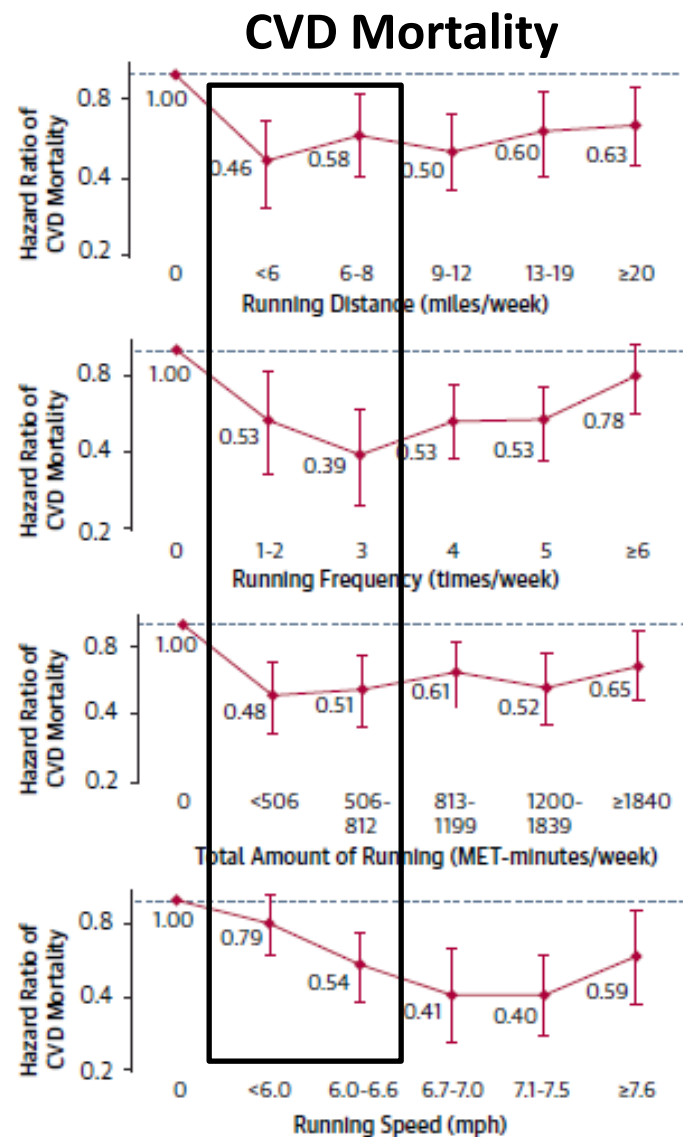
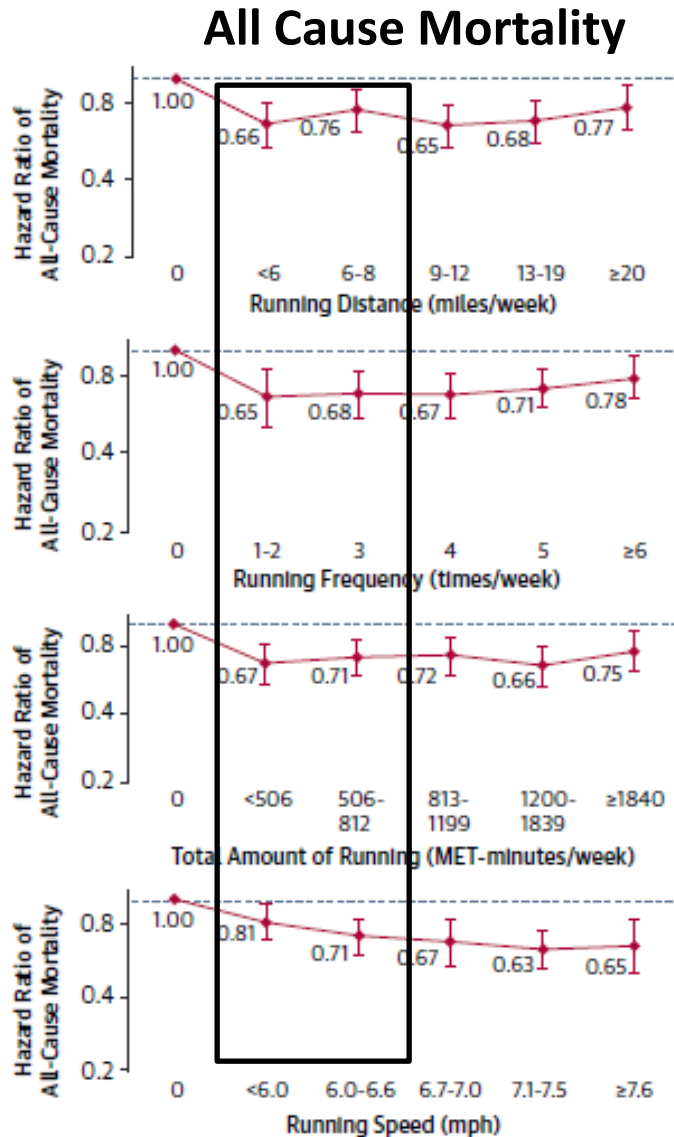
What is the Optimal Dosing Range for Runners?

- 2 early studies that began to shed light on the answer to that question.
 - Lee D-C, Pate RR, Lavie CJ, Sui X, Church TS, Blair SN. Leisure-time running reduces all-cause and cardiovascular mortality risk. *J Am Coll Cardiol.* 2014;64(5):472-481.
 - Schwartz RS, Kraus SM, Schwartz JG, et al. Increased coronary artery plaque volume among male marathon runners. *Mo Medicine* 2014;111(2):85-90.

Affect of Leisure-time Running on All-cause and Cardiovascular Mortality Risk

- Most data on PA and mortality focused on moderate intensity (walking).
- Examined association of running with all-cause and CV mortality risks in 55,137 adults, 18 to 100 yrs. (mean 44 yrs., 26% female); ACLS data.
 - Compared non-runners to runners in 5 quintiles of **distance** (miles/wk), **frequency** (times/wk) , **amount** (MET-min/wk) and **speed** of running (mph).
 - Also looked at effects of a change in running habits over time in sub-group (20,647) who had ≥ 2 exams.

HRs of All-Cause and CV Mortality by Running Distance, Frequency, Total Amount, and Speed



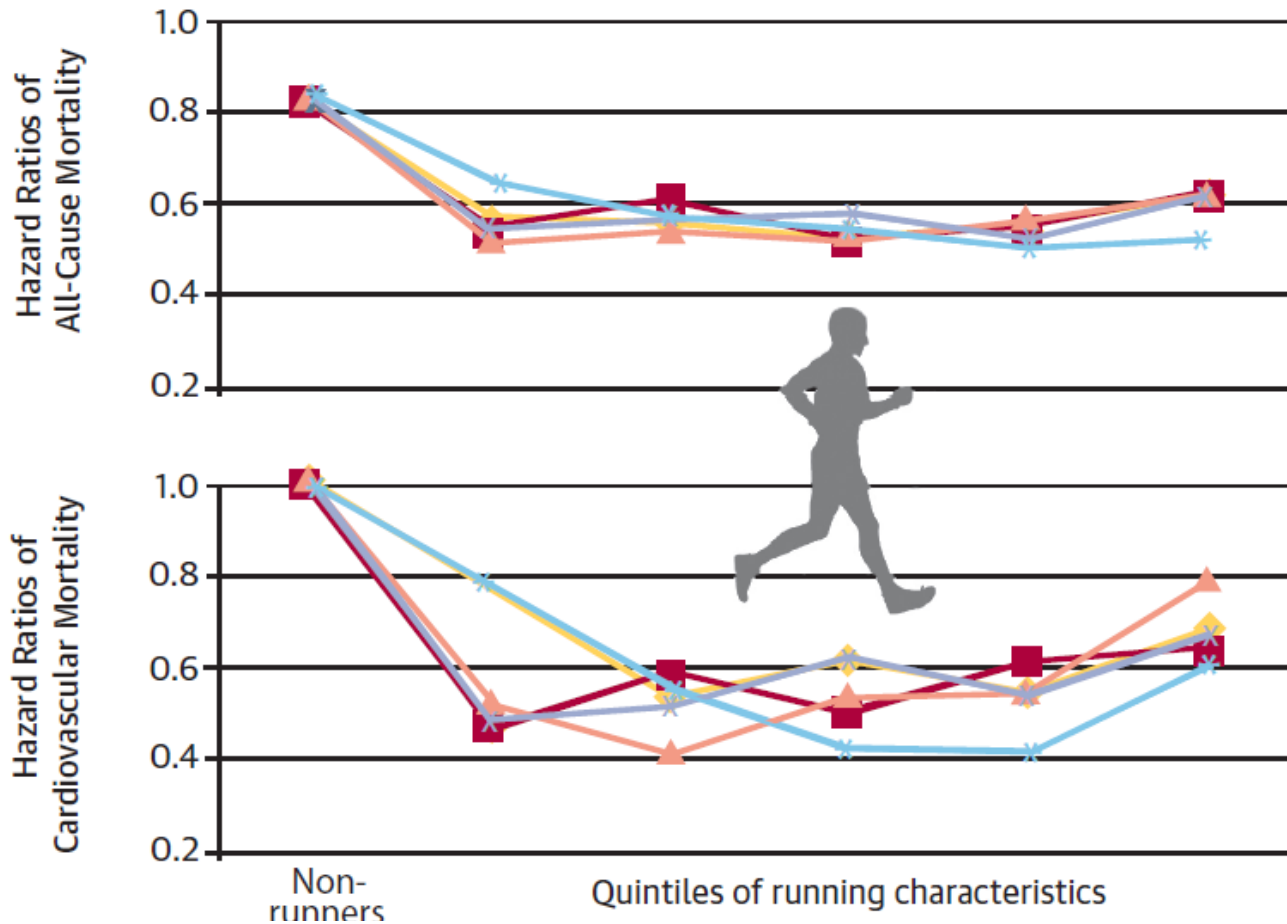
Distance

Frequency

Amount

Speed

Running Reduced All-Cause and CV Mortality Risk

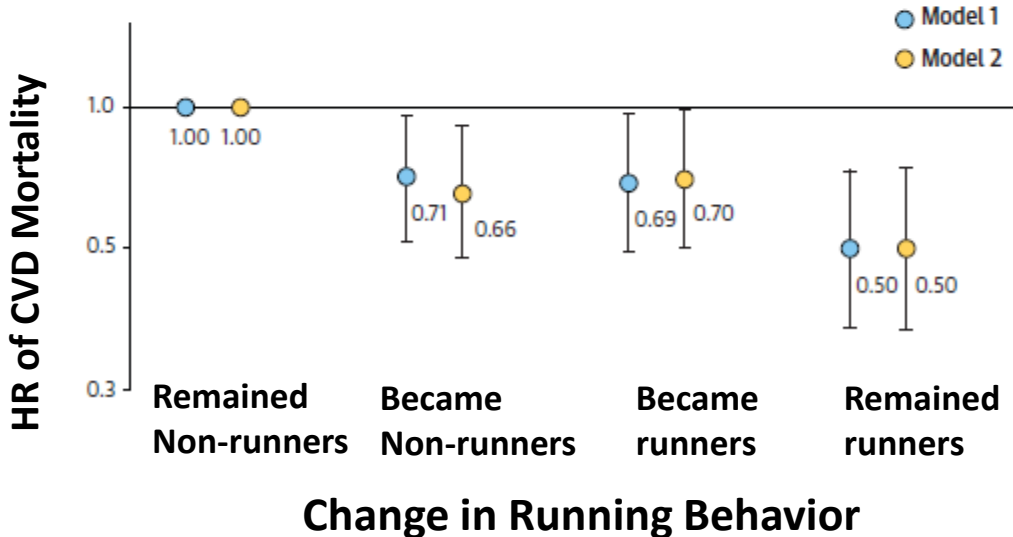


	Non-runners	1	2	3	4	5
Time (min/wk)	0	<51	51-80	81-119	120-175	≥176
Distance (miles/wk)	0	<6	6-8	9-12	13-19	≥20
Frequency (times/wk)	0	1-2	3	4	5	≥6
Total amount (MET-min/wk)	0	<506	506-812	813-1199	1200-1839	≥1840
Speed (mph)	0	<6.0	6.0-6.6	6.7-7.0	7.1-7.5	≥7.6

HRs of All-Cause and Cardiovascular Mortality by Change in Running Behaviors



Model 1 adjusted for age, sex, exam year and interval btw exams.
Model 2 added smoking, alcohol and PA other than running



Lee, et al, *J Am Coll Cardiol*, 2014

Running Study Conclusions

- Runners had consistently lower risk of all-cause and CVD mortality compared with non-runners.
- Running even at lower doses or slower speeds was associated with significant mortality benefits.
 - 30-59 min per week (5-10 min per day) gave significant benefit!
- Persistent running over time was more strongly associated with mortality reduction, but any history of running gave benefit.

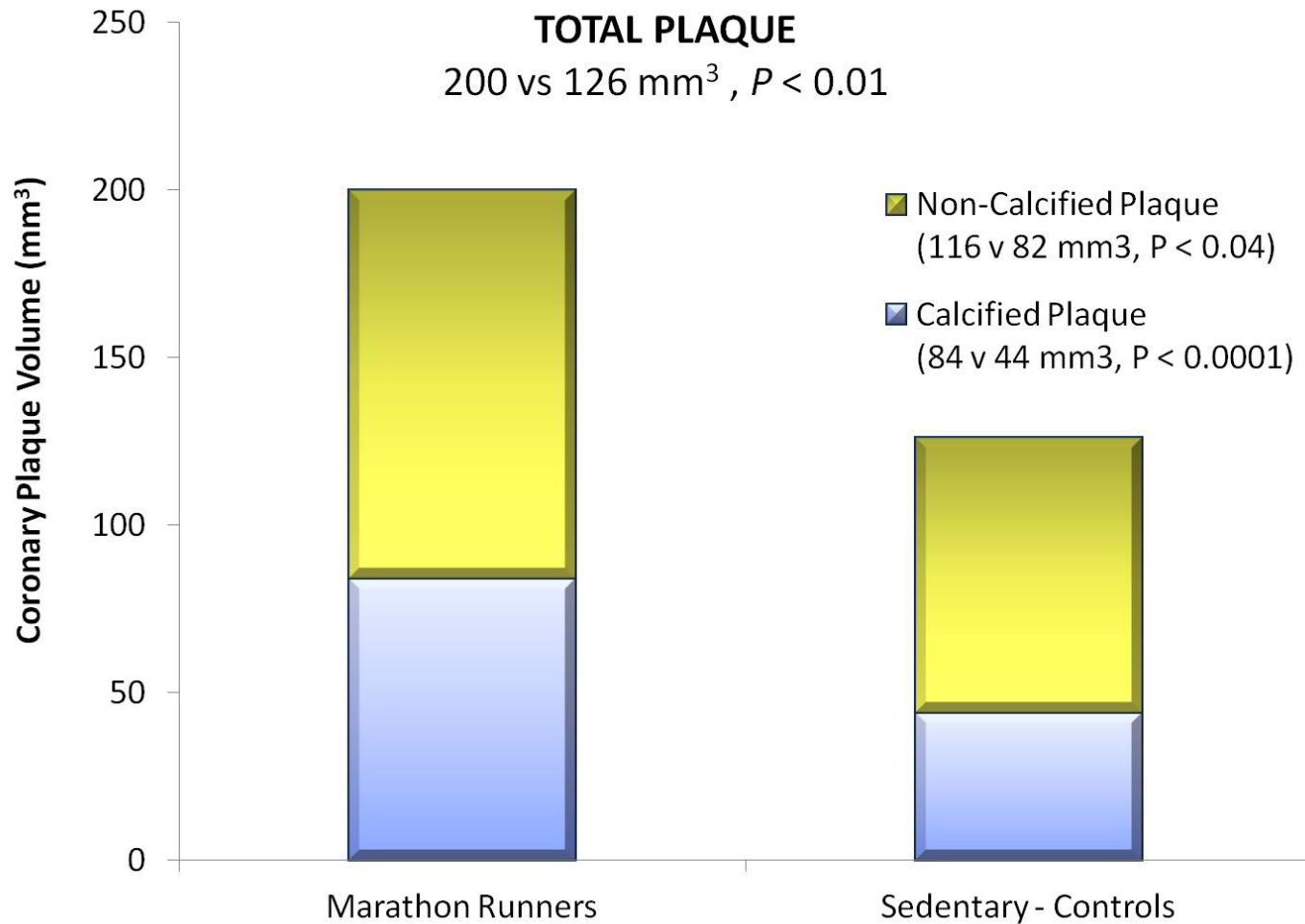
Coronary Artery Plaque Volume Among Male Marathon Runners.

- Most assume marathon running is good for heart health, but many studies suggest otherwise.
- Observational study comparing coronary calcium scores using high sensitivity CCTA in 2 groups of men average age 56-59 yr:
 - 50 male marathon runners (at least 25 marathons done over 25 years).
 - 23 male sedentary controls matched for age and CAD risk factors.
 - Controls had higher resting pulse, weight and BMI, as well as higher rates of high cholesterol, Hypertension and diabetes.

Results

- Male marathon runners had higher:
 - Total plaque volume (200 vs 126 mm²)
 - Calcified plaque volume (84 vs 44 mm²)
 - Non-calcified plaque volume (116 vs 82 mm²)
 - Lesion area and length, number of lesions per subject, and diameter stenosis did not reach statistical significance
- Despite the fact that the marathon runners showed improvement in traditional CV risk factors (lipids, glucose and BMI)

Marathoners showed increased plaque

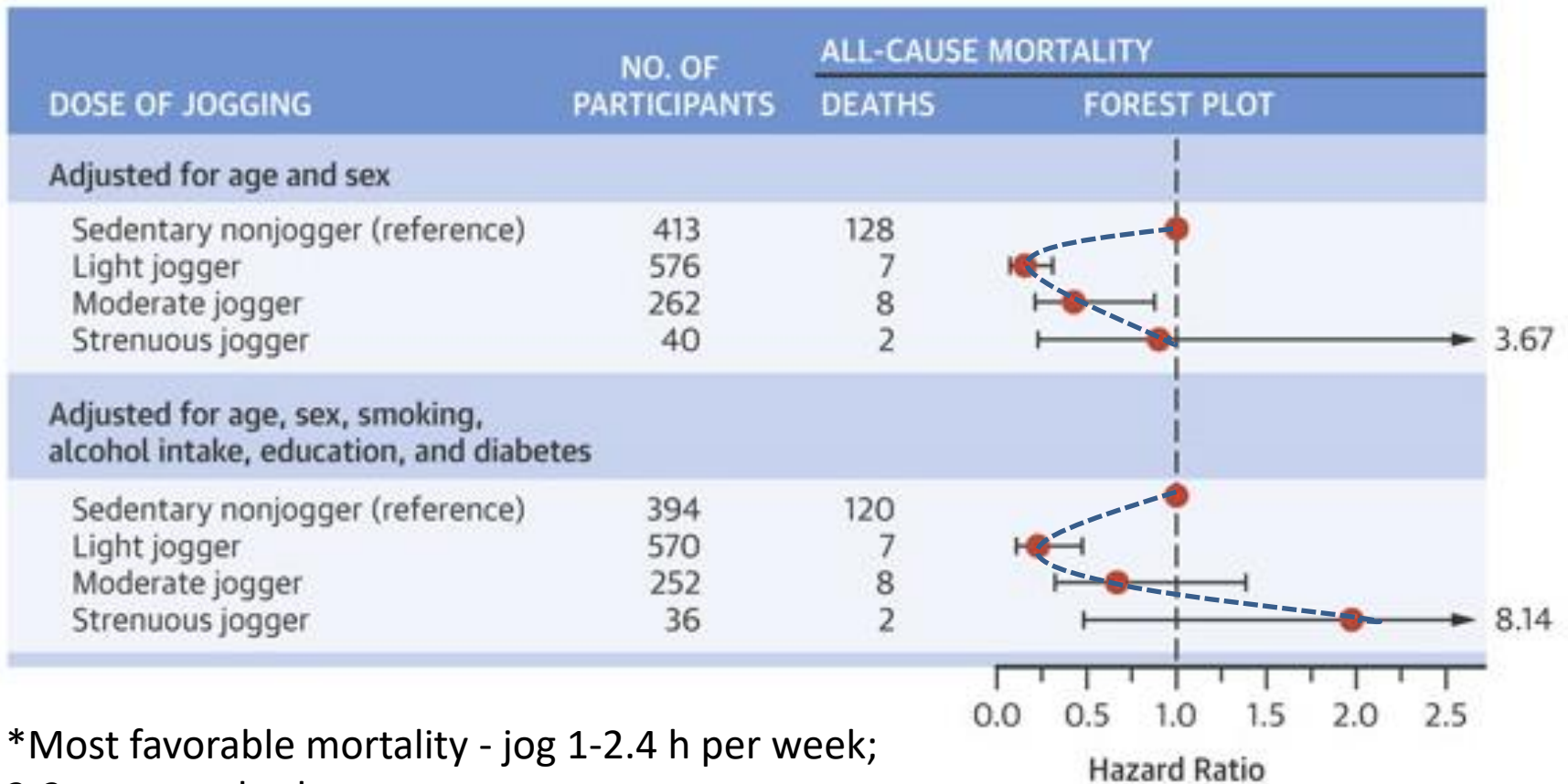


Marathon Study Conclusions

- Long-term male marathon runners may have paradoxically increased coronary artery plaque volume.
- This study lends credence to various observational studies showing dramatic mortality reductions in runners compared with sedentary controls, but the effect seems to follow a U-shaped curve.
- Lowest mortality among runners shown with:
 - Jogging 1-2.5 hours per week at moderate pace; benefit goes away >2.5 hrs. (O’Keefe, Heart, 2013).
 - Jogging 5-20 miles per week; benefit goes away beyond 25 miles per week. (O’Keefe, Heart, 2013).

Dose of Jogging and *Long-Term Mortality*: The Copenhagen City Heart Study

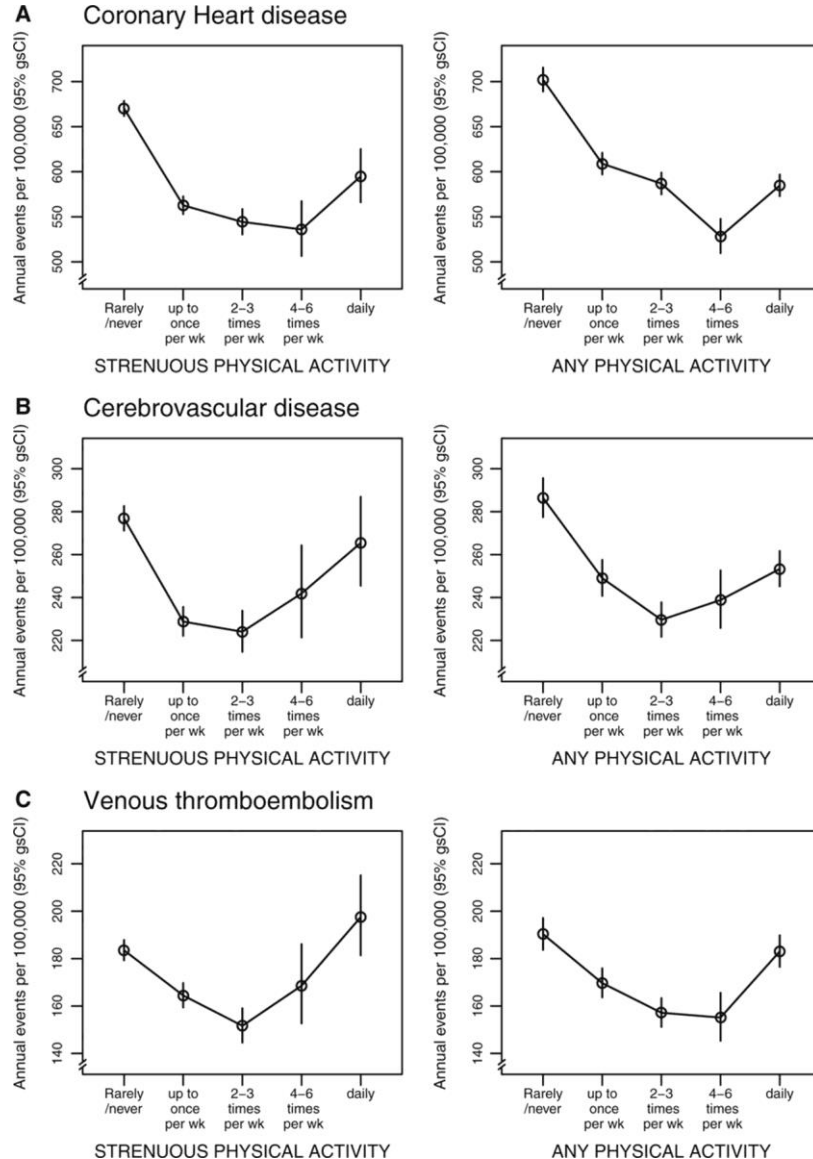
1,098 healthy joggers; 3,950 healthy non-joggers; Prospectively followed 12 years.



*Most favorable mortality - jog 1-2.4 h per week;
2-3x per week; slow to avg. pace

Moderate vs Strenuous PA and CVD Risk

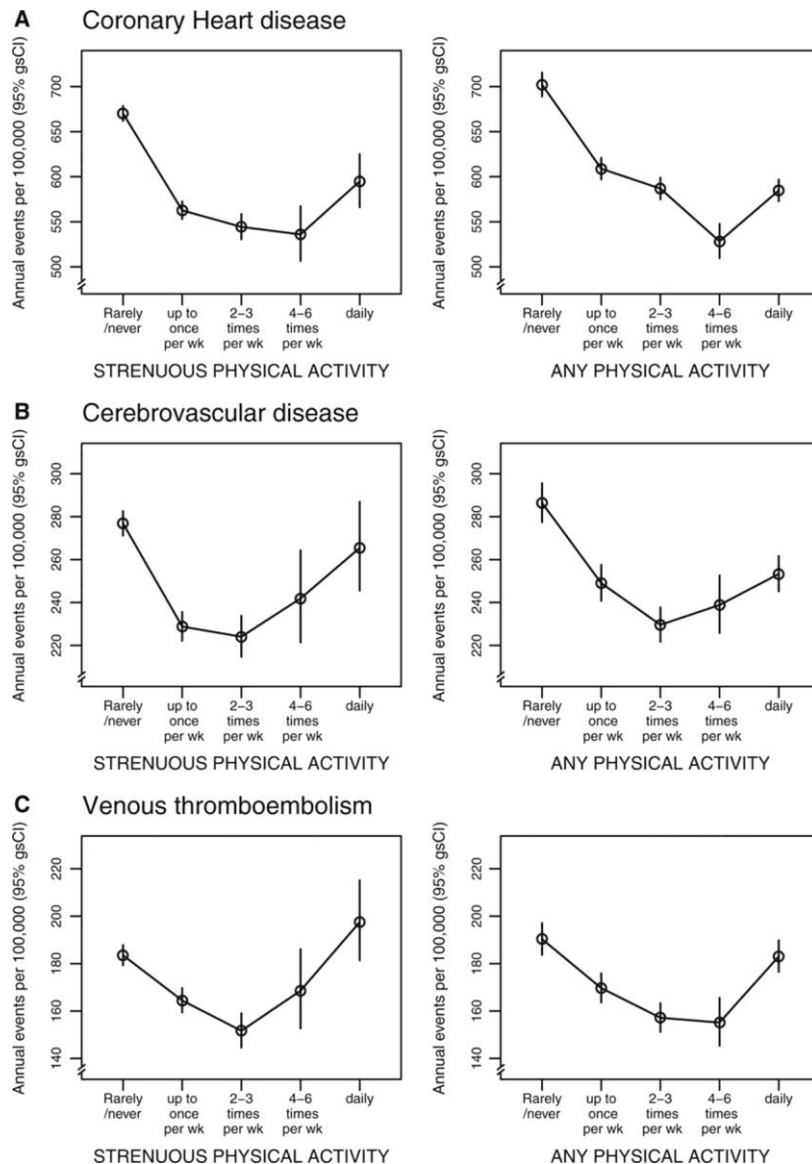
The UK Million Women Study



- Prospective cohort study
- 1.1 million women
 - Age 50 to 64
 - Self reported PA
 - 9 years follow-up
 - 49,113 CHD events
 - 17,822 CVA events
 - 14,550 VTE events
 - Controlled for BMI, smoking, Etoh and SES.

Moderate vs Strenuous PA and CVD Risk

The UK Million Women Study



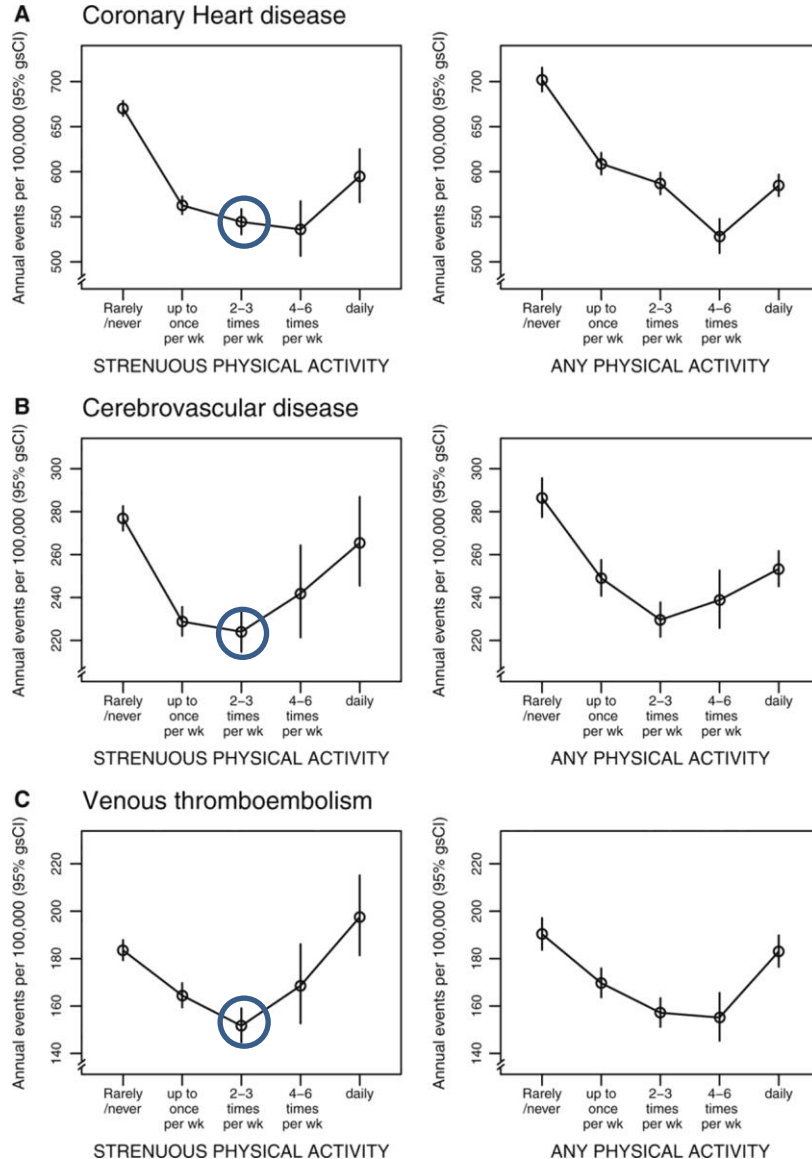
“Goldilocks Zone”

“Sweet Spot”

Strenuous PA; 2-3 times/wk
 Moderate PA; 4-6 times/wk

Moderate vs Strenuous PA and CVD Risk

The UK Million Women Study



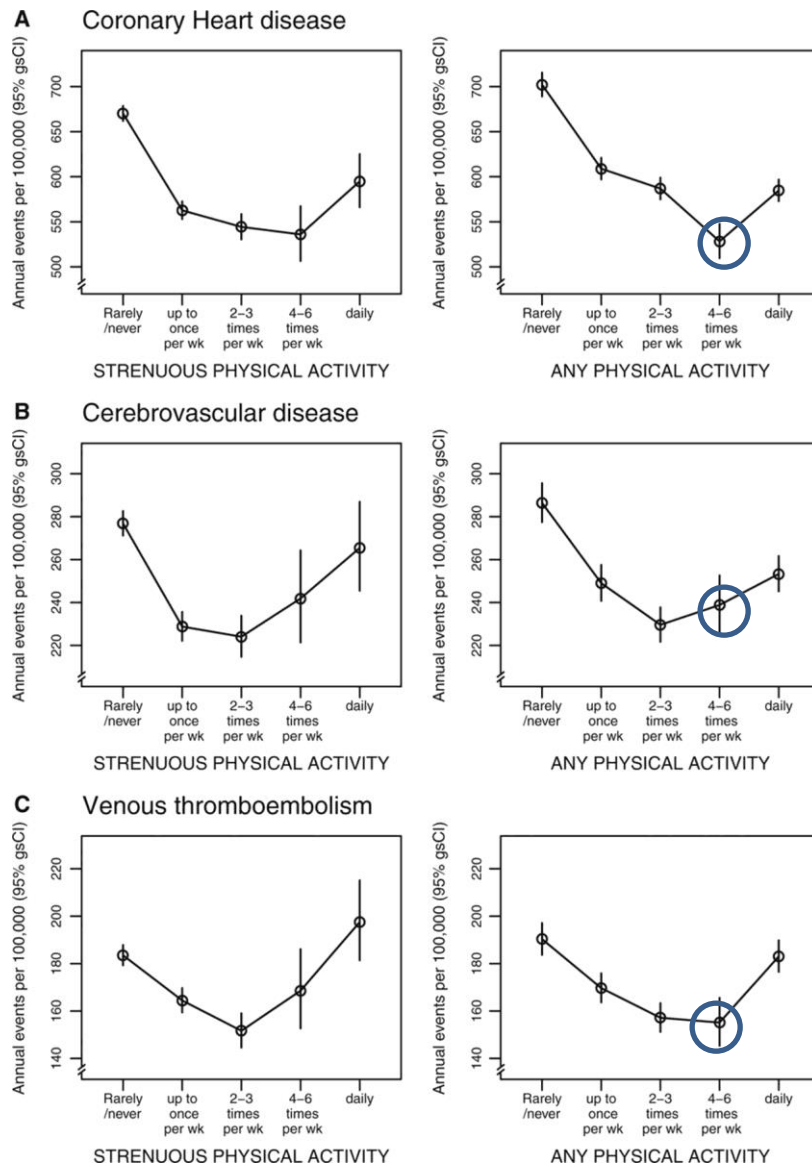
“Goldilocks Zone”

“Sweet Spot”

Strenuous PA; 2-3 times/wk
Moderate PA; 4-6 times/wk

Moderate vs Strenuous PA and CVD Risk

The UK Million Women Study



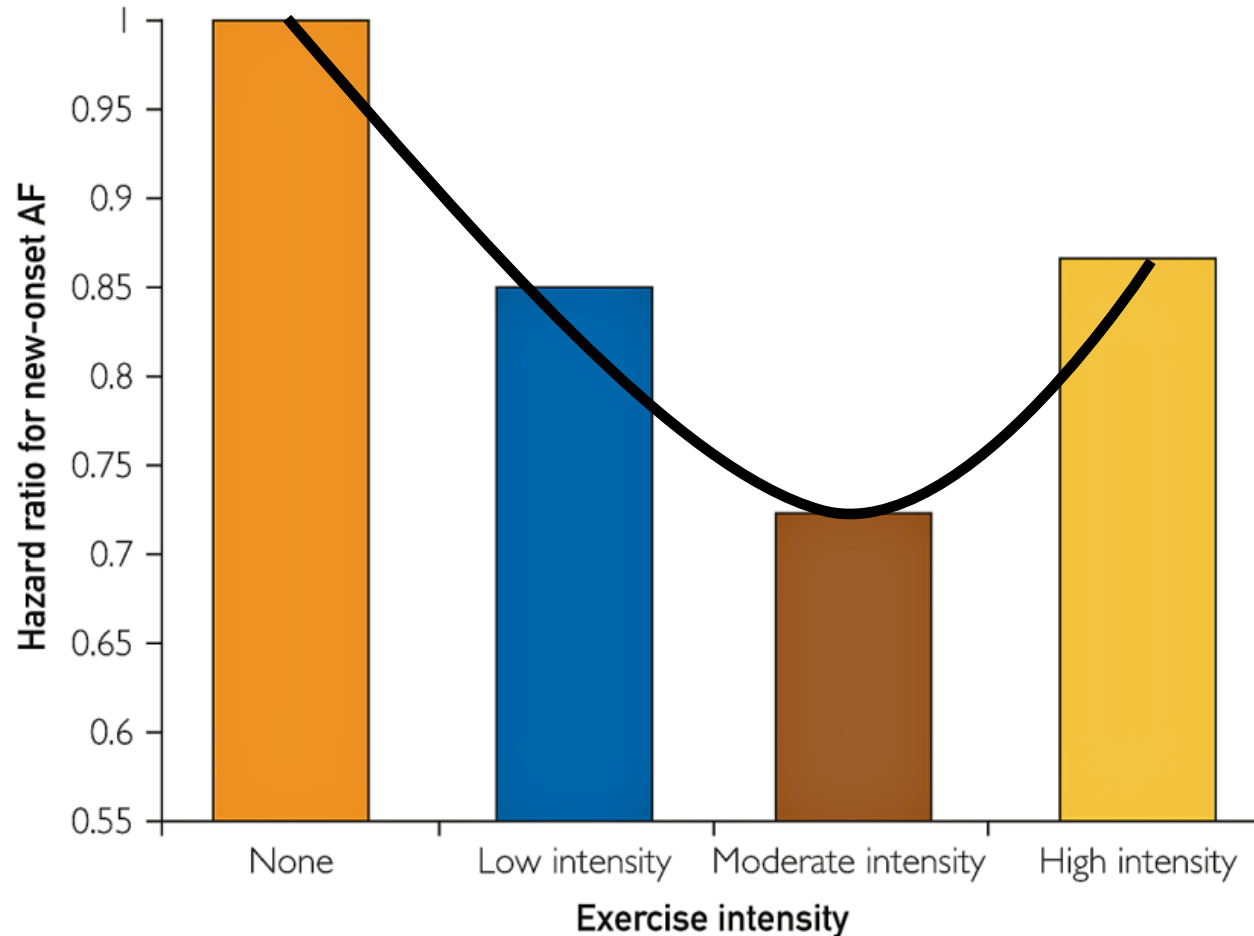
“Goldilocks Zone”

“Sweet Spot”

Strenuous PA; 2-3 times/wk
Moderate PA; 4-6 times/wk

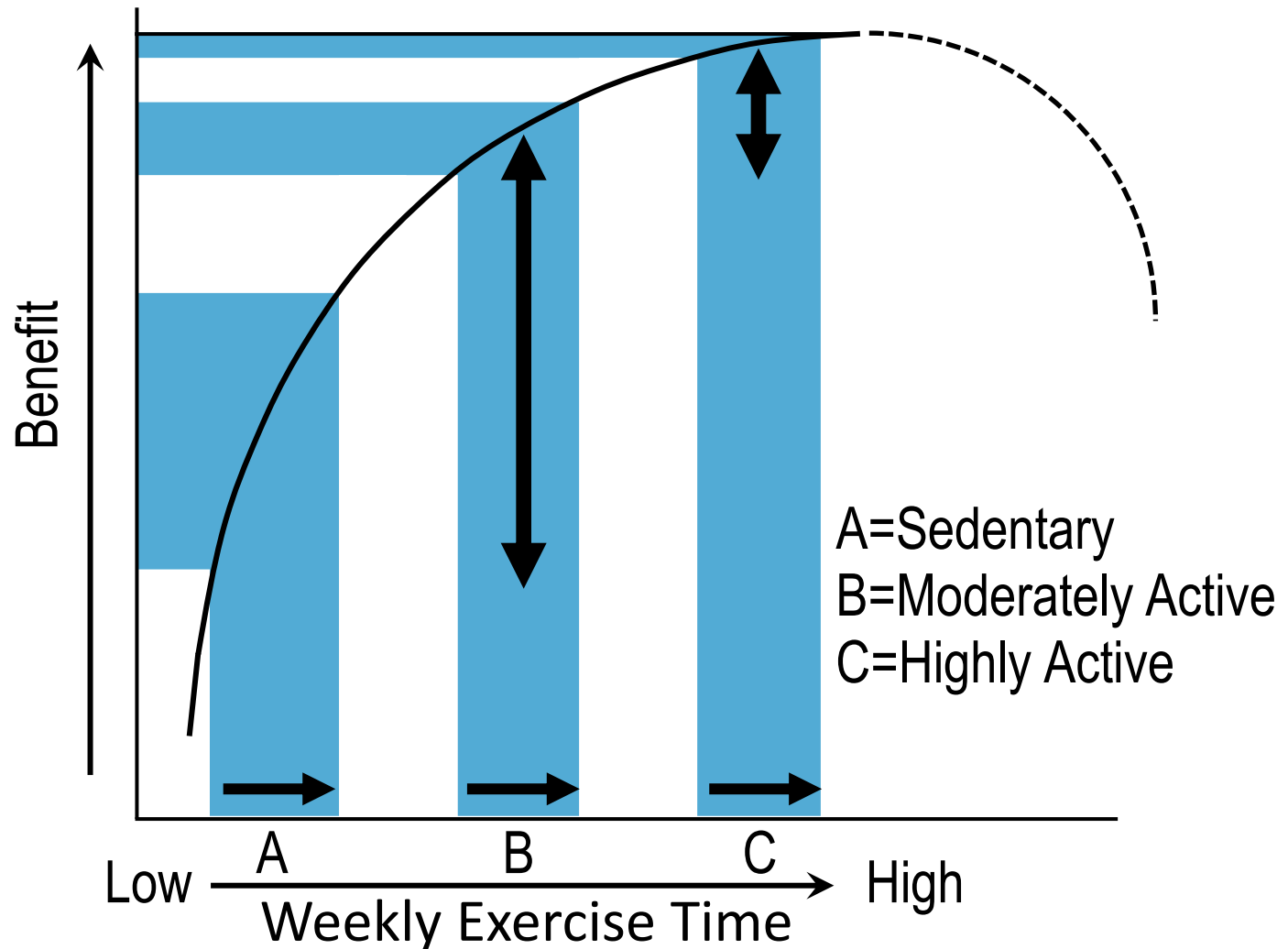
Risk of *A-Fib*

(5446 adults >65 yrs)



Mozaffarian; *Circulation*; 2008

Dose-Response Curve for *Exercise*



Are you surprised?

- Life is about moderation – *if a little is good, more is often not better.*
- Is Athletes Heart really a harmless adaptation?
 - LV enlargement, EKG changes (T-inv, Q-waves, RBBB) and arrhythmia (brady, junctional, AV block).
 - After extreme endurance exercise common to see leak of CPK, Troponin and BNP.
 - Evidence of myocardial fibrosis/scarring, potentially dangerous rhythms, and accelerated CVD.
- Pheidippides' Cardiomyopathy?

My Doctor said "Only 1 glass of alcohol a day". I can live with that.



Are you surprised?

- Life is about moderation – if a little is good, more is often not better.
- Is Athletes Heart really a harmless adaptation?
 - LV enlargement, EKG changes (T-inv, Q-waves, RBBB) and arrhythmia (brady, junctional, AV block).
 - After extreme endurance exercise common to see leak of CPK, Troponin and BNP.
 - Evidence of myocardial fibrosis/scarring, potentially dangerous rhythms, and accelerated CVD.
- Pheidippides' Cardiomyopathy?

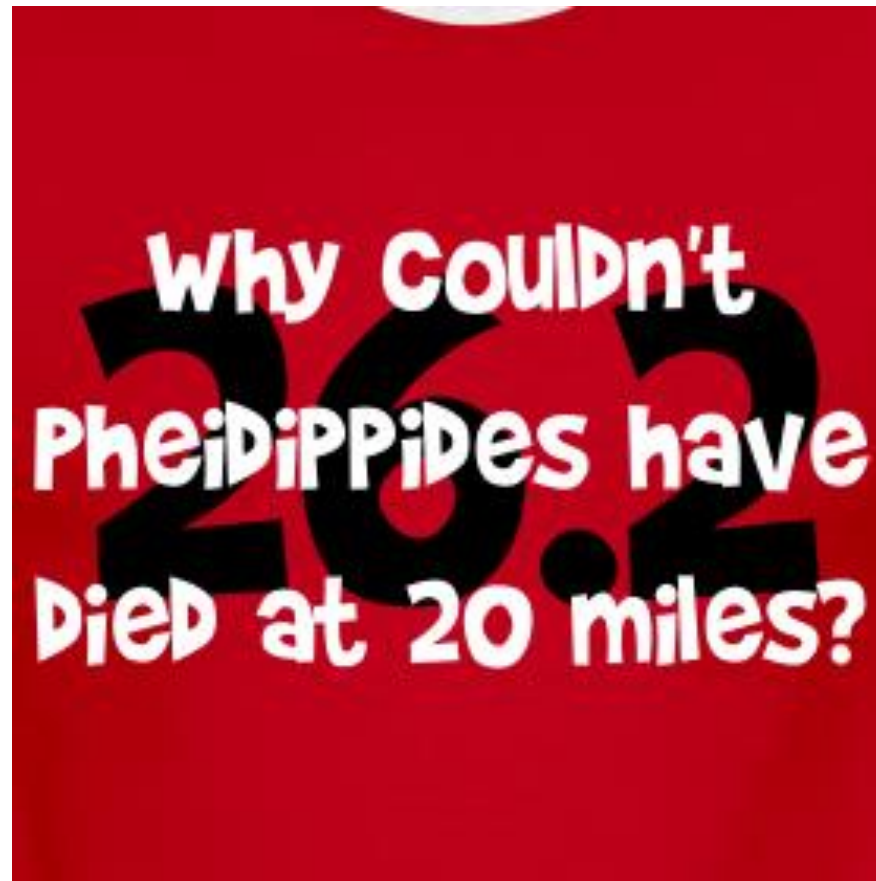
Pheidippides

- Hero of ancient Greece ran 26.2 miles from Marathon to Athens to deliver news of military victory over the Persians.



Pheidippides

- Hero of ancient Greece ran 26.2 miles from Marathon to Athens to deliver news of military victory over the Persians.



Ironman Athletes



A Tale of 2 Patients;

Pick the Heart Patient

- **5'8" Tall**
 - **158 lbs.**
 - **Never drank alcohol**
 - **Low Fat/High Fiber Diet**
 - **Marathon Runner**
 - **Former smoker**
- **5'8" Tall**
 - **270 lbs.**
 - **Heavy drinker**
 - **High Fat/Low Fiber Diet**
 - **Sedentary**
 - **Heavy cigarette and cigar smoker**

Jim Fixx; died age 52 while jogging

- **5'8" Tall**
- **158 lbs.**
- **Never drank alcohol**
- **Low Fat/High Fiber Diet**
- **Marathon Runner**
- **Former smoker**

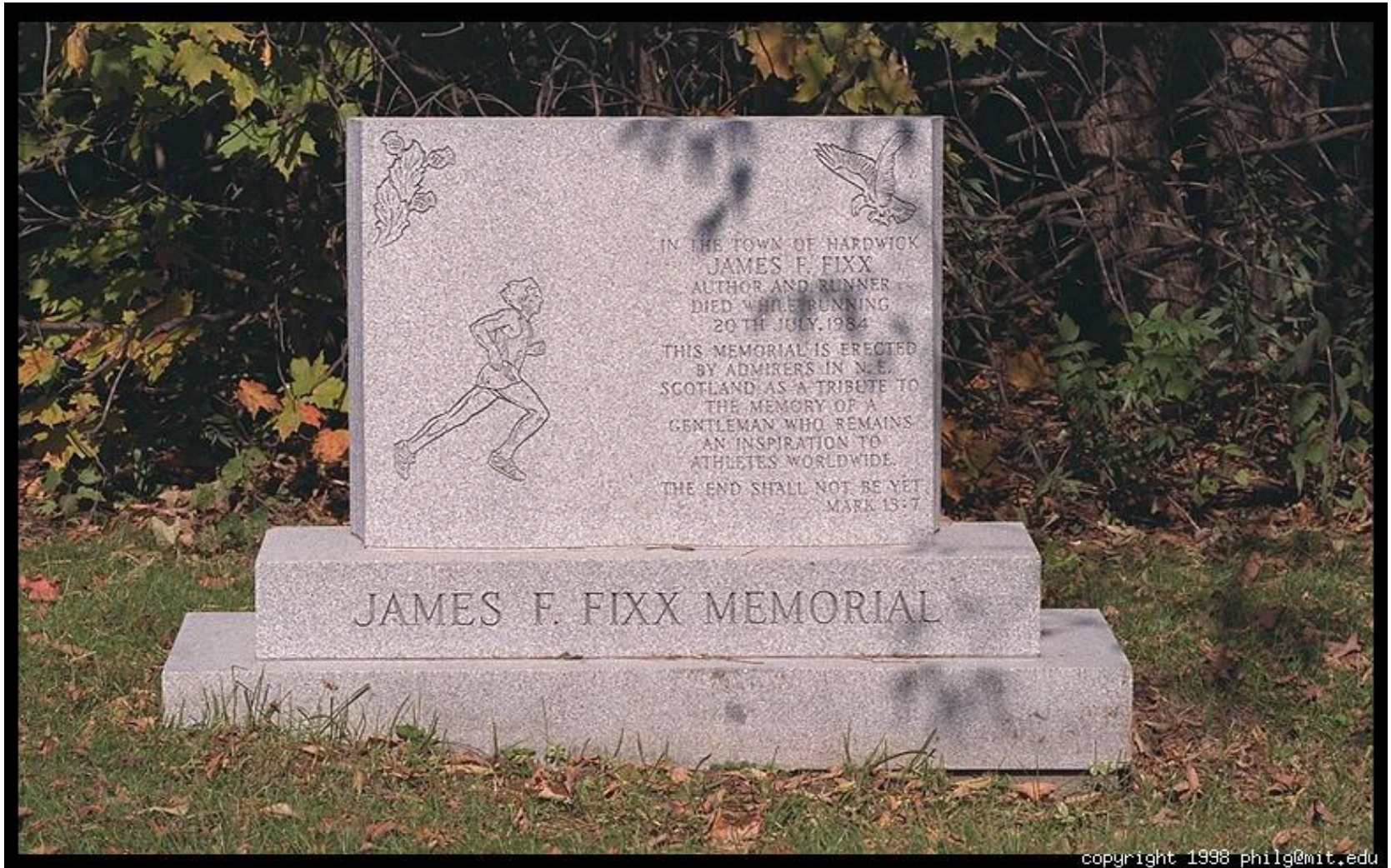


Winton Churchill; died age 90 at home

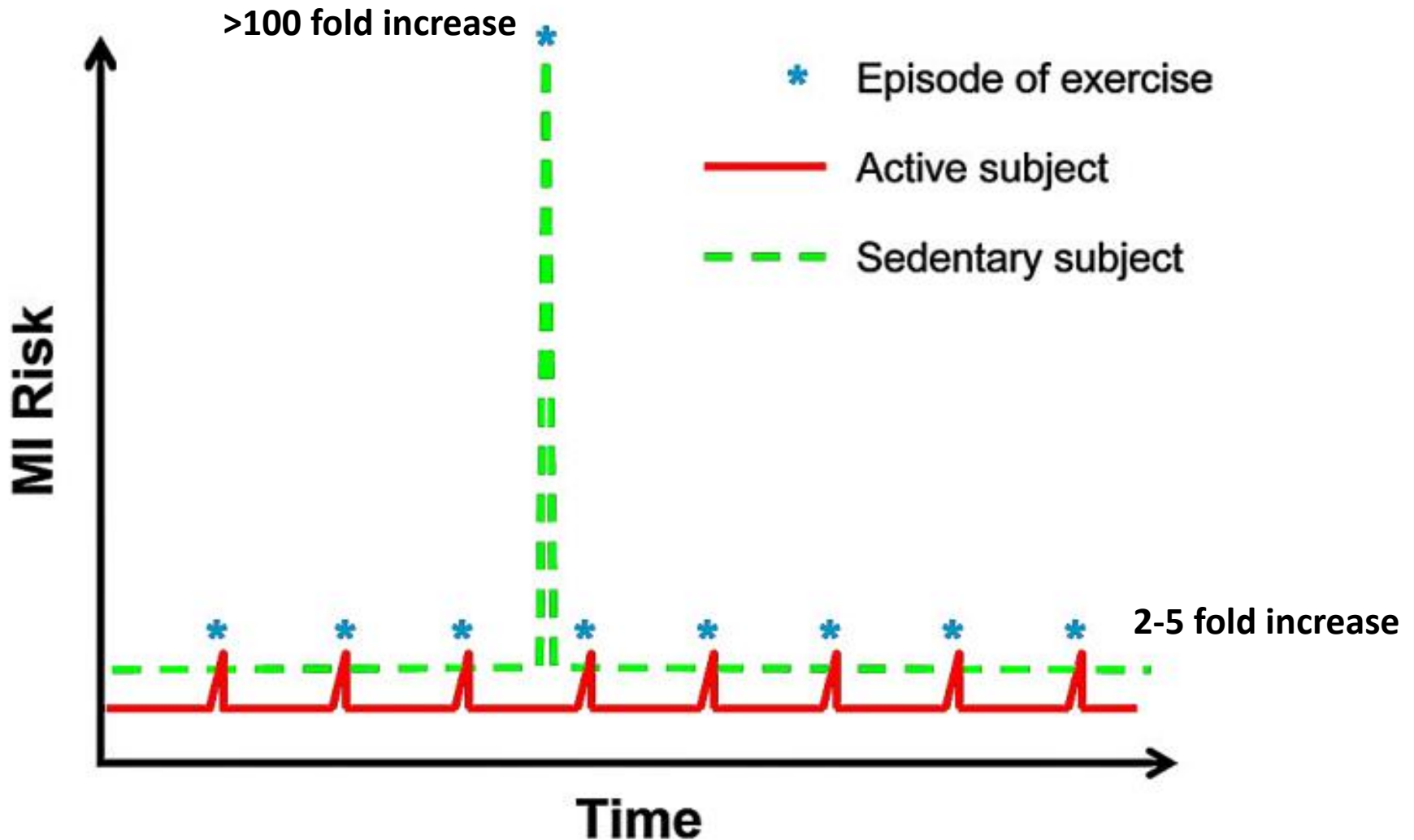


- **5'8" Tall**
- **270 lbs.**
- **Heavy drinker**
- **High Fat/Low Fiber Diet**
- **Sedentary**
- **Heavy cigarette and cigar smoker**

Sometimes you cannot outrun your genes!



MI Risk with *Exercise*



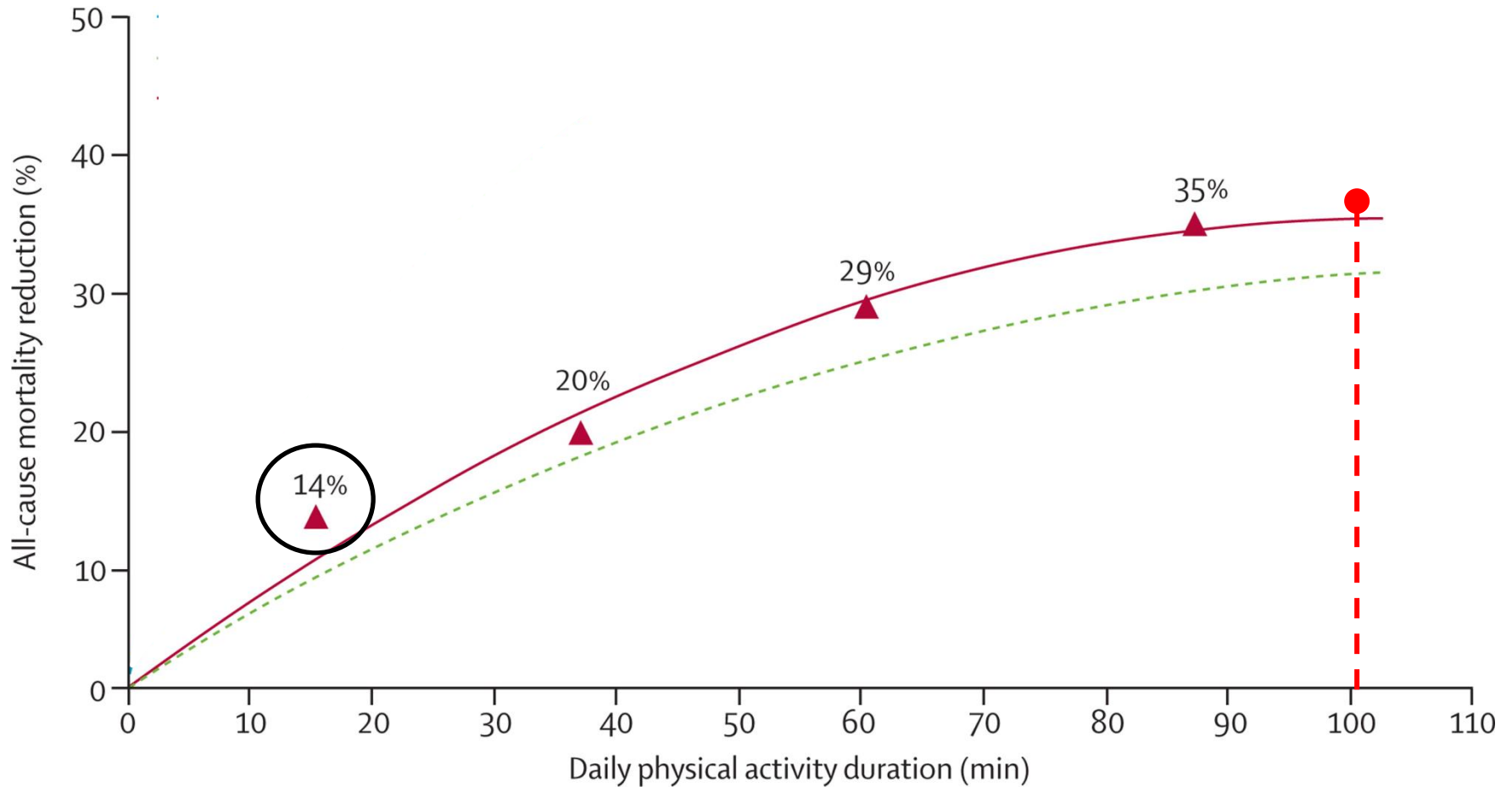
How about walking?



What is the Optimal Dosing Range for **Walkers**?

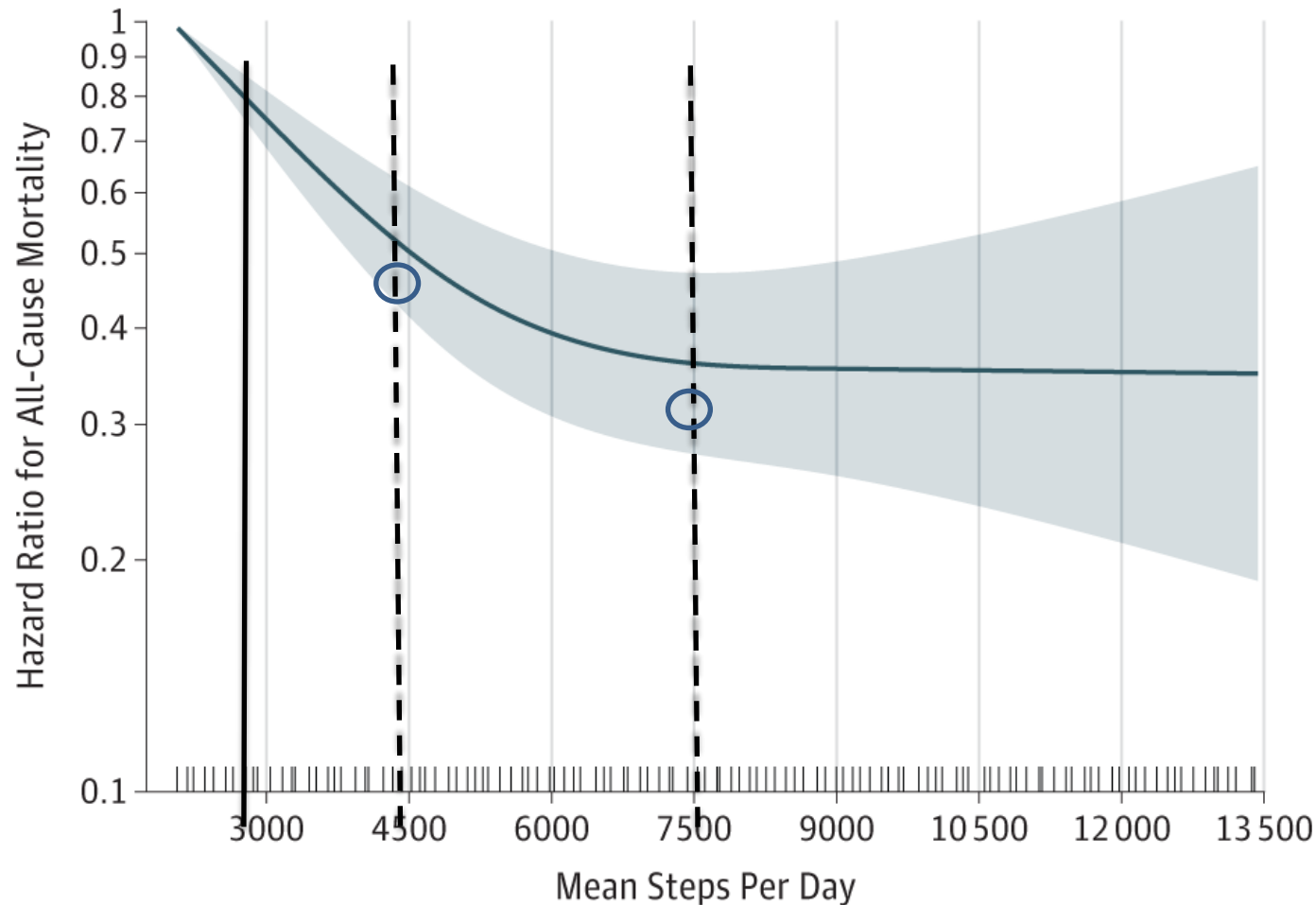
- 416,175 adults in Taiwan; Followed 8.5 years with activity questionnaires; Correlated with mortality rates
- Compared to inactive group, those doing 92 min per week (~15 min per day) walking:
 - Reduced mortality by 14%
 - 3 years longer life expectancy
 - Every 15 min per day walking, further reduced mortality by 4% (up to 100 min per day)
- Applied to both men and women

How much does walking reduce *mortality*?



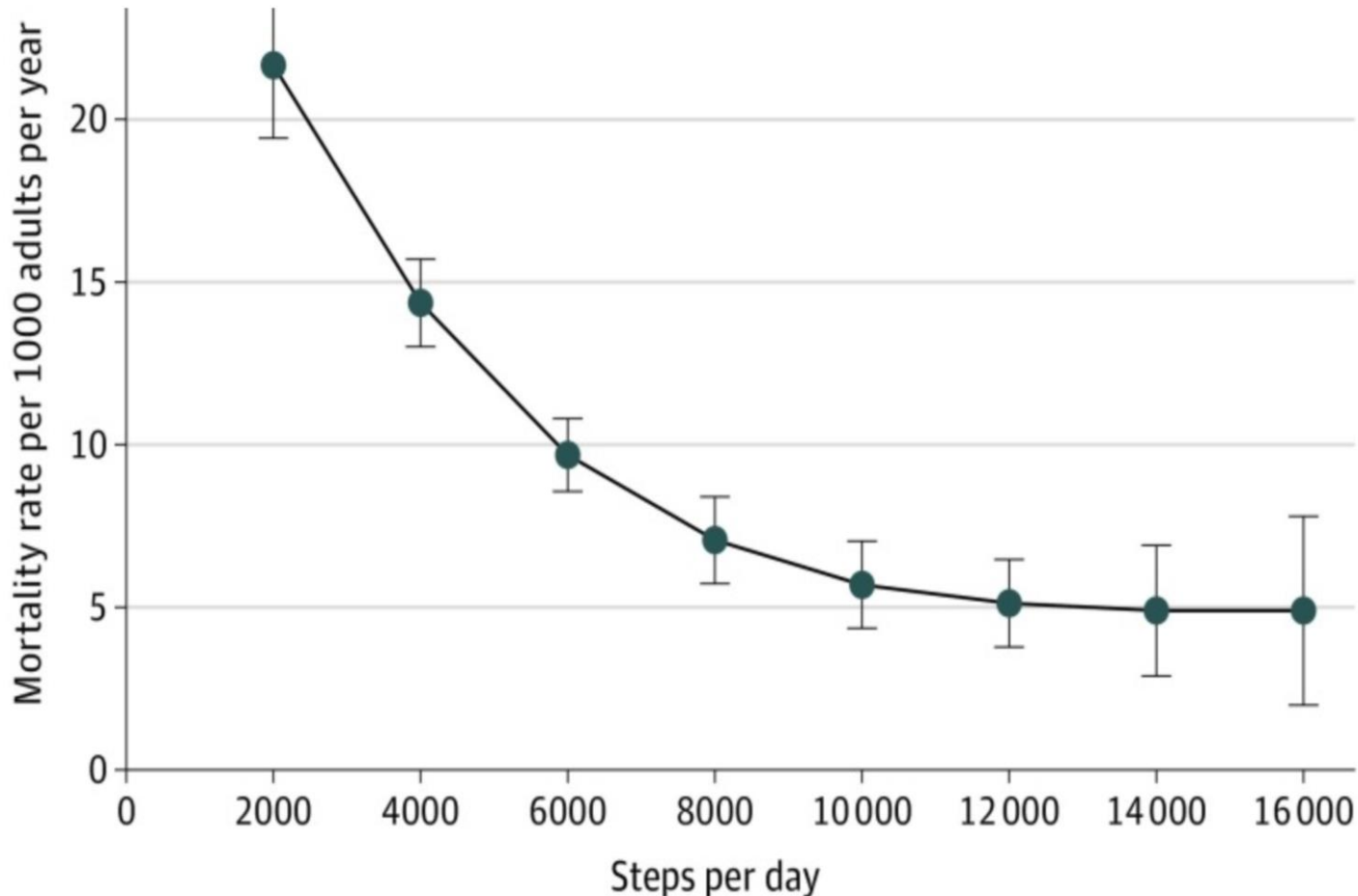
Wen CP, et al; Lancet, 2011

It Doesn't Take a lot of Steps!



- 16,741 women
- Mean age of 72 yrs followed 4.3 yrs.
- Those averaging **~4400 steps/d** had significantly lower mortality compared to **~2700 steps/d**
- Mortality rates progressively decreased before leveling at approx **7500 steps/d**.
- Step Intensity not related to mortality

Association of Daily Step Counts and Mortality



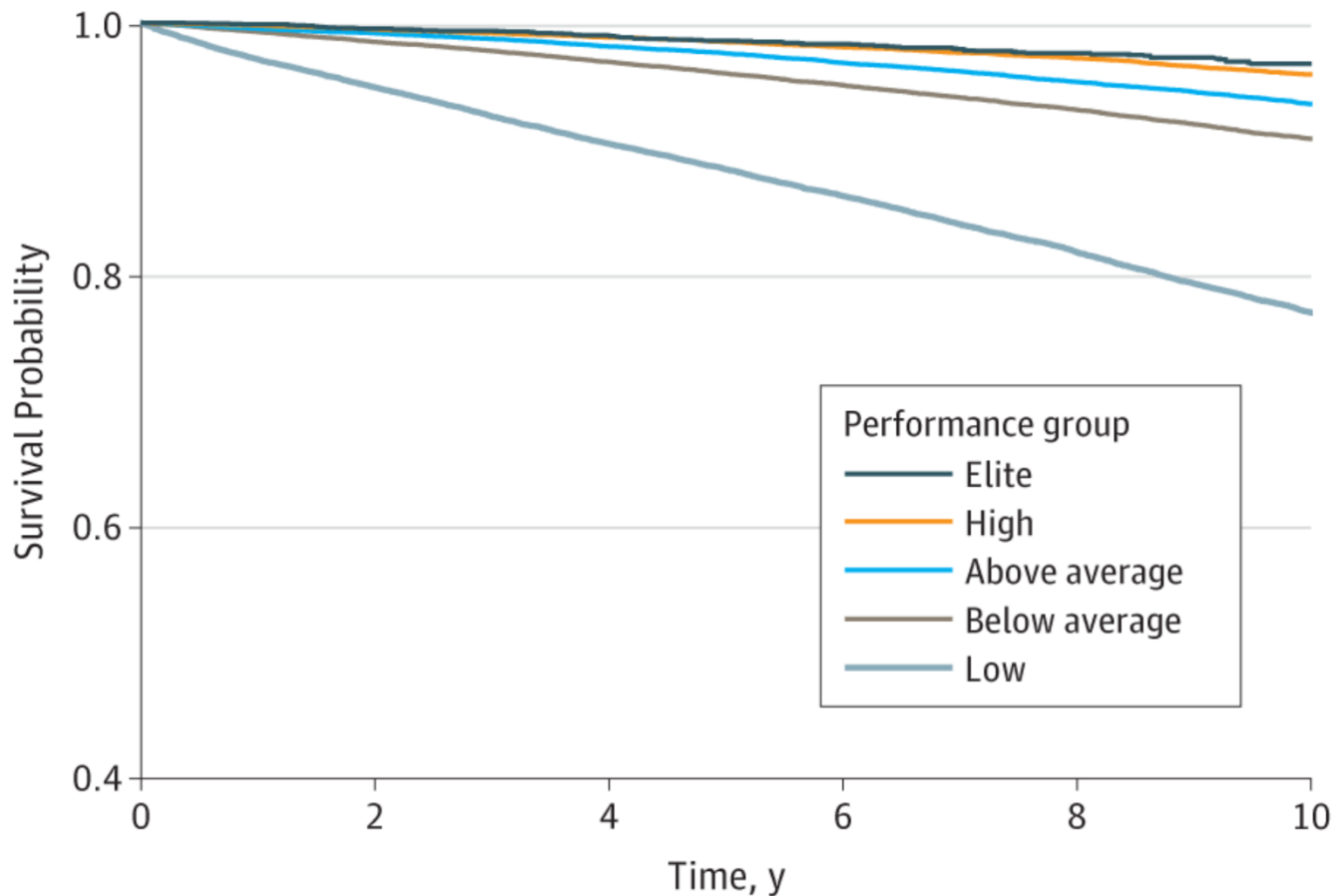
- 4440 Adults
- Mean age 57y
- Accelerometer x 7d to measure steps & intensity.
- No association btw intensity and mortality

How fast do you need to walk; To stay ahead of the Grim Reaper?



- Several studies have shown correlation between walking speed and survival.
- 1705 Australia men, age ≥ 70 ; Measured walking speed at usual pace for 6 m (~20 feet); Speed correlated with mortality rates over 5 yrs:
 - Walking speed of 0.82 m/s (2 mph or 3 kph) was most predictive of mortality (i.e. speed of Grim Reaper)
 - No men walking at speeds ≥ 1.36 m/s (3 mph or 5 kph) were caught by Grim Reaper
- Walking faster protects against mortality!

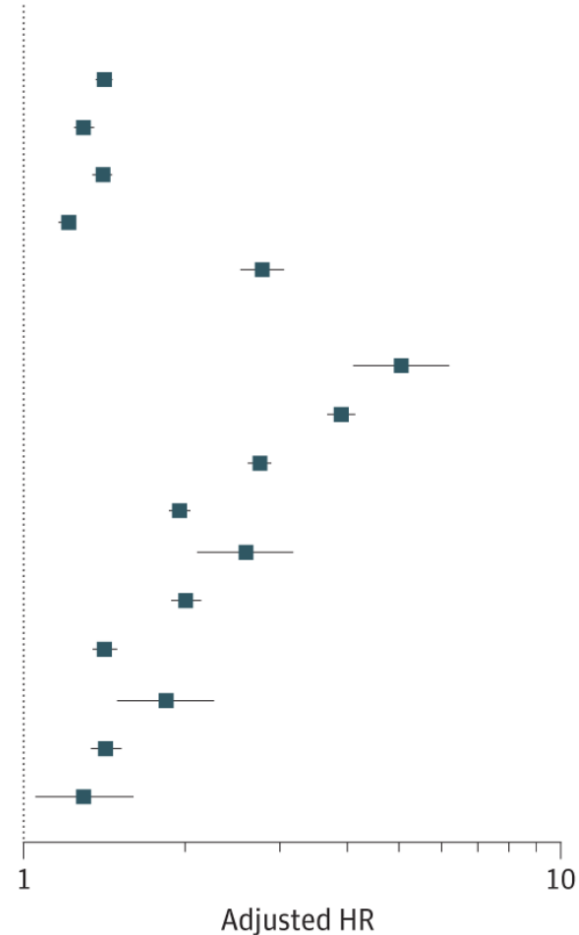
Association of Fitness With Mortality in Adults Undergoing Ex Treadmill Testing



**-122,007 adults with ETT at Clev Clinic
-1991-2014 (23 yrs)
-Fitness inversely a/w all-cause mortality in 5 quintiles of fitness**

Low Fitness Was Bigger Risk than Hypertension, Diabetes, CAD or *Smoking*

Variable	HR (95% CI)	P Value
Comorbidity		
Smoking	1.41 (1.36-1.46)	<.001
CAD	1.29 (1.24-1.35)	<.001
Diabetes	1.40 (1.34-1.46)	<.001
Hypertension	1.21 (1.16-1.25)	<.001
ESRD	2.78 (2.53-3.05)	<.001
Group comparison		
Low vs Elite	5.04 (4.10-6.20)	<.001
Low vs High	3.90 (3.67-4.14)	<.001
Low vs Above Average	2.75 (2.61-2.89)	<.001
Low vs Below Average	1.95 (1.86-2.04)	<.001
Below Average vs Elite	2.59 (2.10-3.19)	<.001
Below Average vs High	2.00 (1.88-2.14)	<.001
Below Average vs Above Average	1.41 (1.34-1.49)	<.001
Above Average vs Elite	1.84 (1.49-2.26)	<.001
Above Average vs High	1.42 (1.33-1.52)	<.001
High vs Elite	1.29 (1.05-1.60)	.02



High Levels of PA Linked to Increased CAC but NOT Mortality

- 21,758 healthy men (mean age 51.7 yr) reported PA, had CAC screening and 10 yr f/u.
- ≥ 3000 MET-min/wk more likely to have CAC ≥ 100 AU.
- No increase in all-cause or CVD mortality

Research

JAMA Cardiology | Original Investigation

Association of All-Cause and Cardiovascular Mortality With High Levels of Physical Activity and Concurrent Coronary Artery Calcification

Laura F. DeFina, MD; Nina B. Radford, MD; Carolyn E. Barlow, PhD; Benjamin L. Willis, MD, MPH; David Leonard, PhD; William L. Haskell, PhD; Stephen W. Farrell, PhD; Anđjelka Pavlovic, PhD; Katelyn Abel, Jarett D. Berry, MD; Amit Khara, MD, MSc; Benjamin D. Levine, MD

IMPORTANCE Few data are available to guide clinical recommendations for individuals with high levels of physical activity in the presence of clinically significant coronary artery calcification (CAC).

OBJECTIVE To assess the association among high levels of physical activity, prevalent CAC, and subsequent mortality risk.

DESIGN, SETTING, AND PARTICIPANTS The Cooper Center Longitudinal Study is a prospective observational study of patients from the Cooper Clinic, a preventive medicine facility. The present study included participants seen from January 13, 1998, through December 30, 2013, with mortality follow-up through December 31, 2014. A total of 21 758 generally healthy men without prevalent cardiovascular disease (CVD) were included if they reported their physical activity level and underwent CAC scanning. Data were analyzed from September 26, 2017, through May 2, 2018.

EXPOSURES Self-reported physical activity was categorized into at least 3000 (n = 1561), 1500 to 2999 (n = 3750), and less than 1500 (n = 16 447) metabolic equivalent of task (MET)-minutes/week (min/wk). The CAC scores were categorized into at least 100 (n = 5314) and less than 100 (n = 16 444) Agatston units (AU).

MAIN OUTCOMES AND MEASURES All-cause and CVD mortality collected from the National Death Index Plus.

RESULTS Among the 21 758 male participants, baseline mean (SD) age was 51.7 (8.4) years. Men with at least 3000 MET-min/wk were more likely to have prevalent CAC of at least 100 AU (relative risk, 1.1; 95% CI, 1.03-1.20) compared with those accumulating less physical activity. In the group with physical activity of at least 3000 MET-min/wk and CAC of at least 100 AU, mean (SD) CAC level was 807 (1120) AU. After a mean (SD) follow-up of 10.4 (4.3) years, 759 all-cause and 180 CVD deaths occurred, including 40 all-cause and 10 CVD deaths among those with physical activity of at least 3000 MET-min/wk. Men with CAC of less than 100 AU and physical activity of at least 3000 MET-min/wk were about half as likely to die compared with men with less than 1500 MET-min/wk (hazard ratio [HR], 0.52; 95% CI, 0.29-0.91). In the group with CAC of at least 100 AU, men with at least 3000 MET-min/wk did not have a significant increase in all-cause mortality (HR, 0.77; 95% CI, 0.52-1.15) when compared with men with physical activity of less than 1500 MET-min/wk. In the least active men, those with CAC of at least 100 AU were twice as likely to die of CVD compared with those with CAC of less than 100 AU (HR, 1.93; 95% CI, 1.34-2.78).

CONCLUSIONS AND RELEVANCE This study suggests there is evidence that high levels of physical activity (≥ 3000 MET-min/wk) are associated with prevalent CAC but are not associated with increased all-cause or CVD mortality after a decade of follow-up, even in the presence of clinically significant CAC levels.

JAMA Cardiol. doi:10.1001/jamacardio.2018.4628
Published online January 30, 2019.

Author Affiliations: Research Division, The Cooper Institute, Dallas, Texas (DeFina, Barlow, Willis, Leonard, Farrell, Pavlovic, Abel); Department of Cardiovascular Medicine, Cooper Clinic, Dallas, Texas (Radford); Department of Medicine, Stanford University, Stanford, California (Haskell); Division of Cardiology, Department of Medicine, University of Texas Southwestern Medical Center, Dallas (Berry, Khara, Levine); Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital, Dallas (Levine).

Corresponding Author: Benjamin D. Levine, MD, Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital, 7232 Greenville Ave, Ste 435, Dallas, TX 75231 (benjaminlevine@texashealth.org).

© 2019 American Medical Association. All rights reserved.

Summary

- Exercise is Medicine that can extend life; Running & walking are great formulations.
- Like any medicine, it has an optimal dosage range, as well as sub-therapeutic and toxic ranges.
 - Running as little as 60 min per week (10 min; 6 days a week) has significant benefits.
 - Walking as little as 92 min per week (15 min; 6 days a week) has significant benefits.
 - Running >2.5 hours per week or >25 miles per week does not seem to provide health benefit and may be harmful.
 - Walking beyond 100 min per day does not seem to add benefit.
 - Extreme endurance exercise may be hazardous to heart.

Summary (continued)

- Various studies support the recommendations from the US Physical Activity Guidelines:
 - 150 min per week of moderate exercise (like brisk walk) and 60 min per day in kids.
 - 75 minutes per week of vigorous exercise (like jogging).
- Biggest benefit is going from sedentary to just moderate amounts of exercise.
- Risk of sudden death goes up with exercise, but especially in sedentary individuals.
- Don't forget the significant health benefits from strength and flexibility training.

Questions?



**I've been running for about 10 minutes.
I'm pretty tired, I think I'll go home now...**