Exercise Paradox

Indice

- Premessa generale
- Definizione
- Metodologia
- Evidenze in letteratura “a sostegno” di EP
- Evidenze in letteratura che “non sostengono” EP
- Limiti delle evidenze
- Conclusioni

Conflitto di interesse

- **Nulla da dichiarare**

Paradosso

- Un **paradosso**, dal greco *παρά* (*contro*) e *δόξα* (*opinione*), è, genericamente, la **descrizione di un fatto che contraddice l'opinione comune** o l'esperienza quotidiana, **riuscendo perciò sorprendente**, straordinaria o bizzarra.

French paradox

- Per **paradosso francese** si intende il presunto fenomeno per il quale in Francia, nonostante il relativamente alto consumo di alimenti ricchi in acidi grassi saturi, l'incidenza di mortalità per malattie cardiovascolari è relativamente bassa, inferiore rispetto ad altri Paesi dieteticamente comparabili.
- Su tale apparente paradosso si è speculato che il consumo di vino rosso potesse proteggere da malattie cardiache.

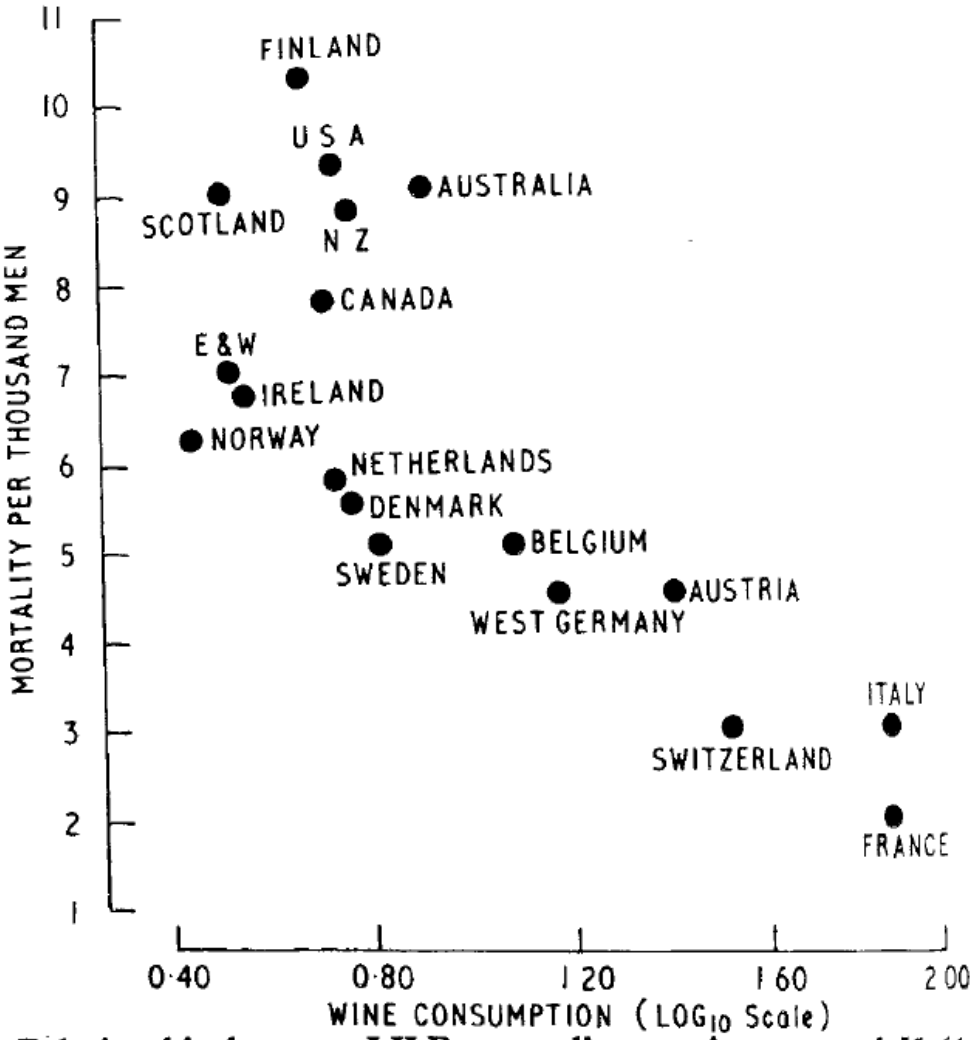
THE LANCET, MAY 12, 1979

Public Health

FACTORS ASSOCIATED WITH CARDIAC MORTALITY IN DEVELOPED COUNTRIES WITH PARTICULAR REFERENCE TO THE CONSUMPTION OF WINE

A. S. ST. LEGER A. L. COCHRANE*
F. MOORE

Medical Research Council Epidemiology Unit, Cardiff CF2 3AS



Relationship between I.H.D. mortality-rate in men aged 55–64 and wine consumption.

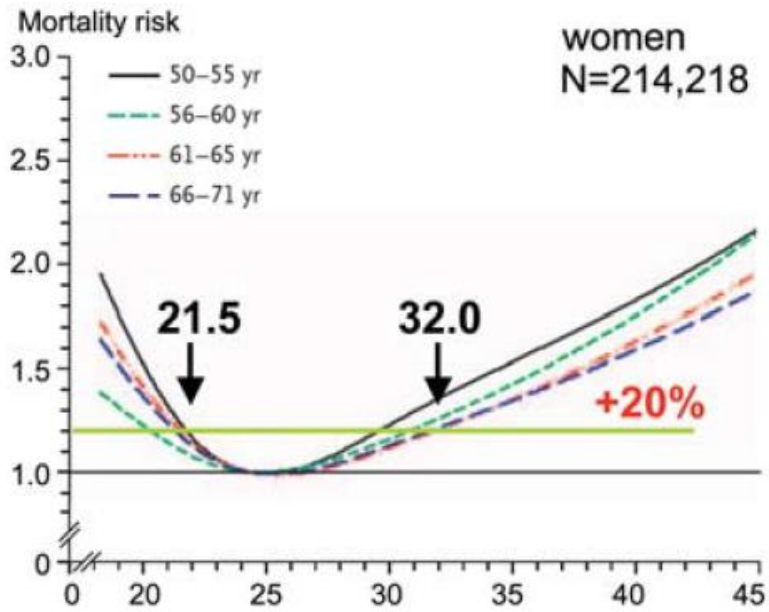
Obesity paradox

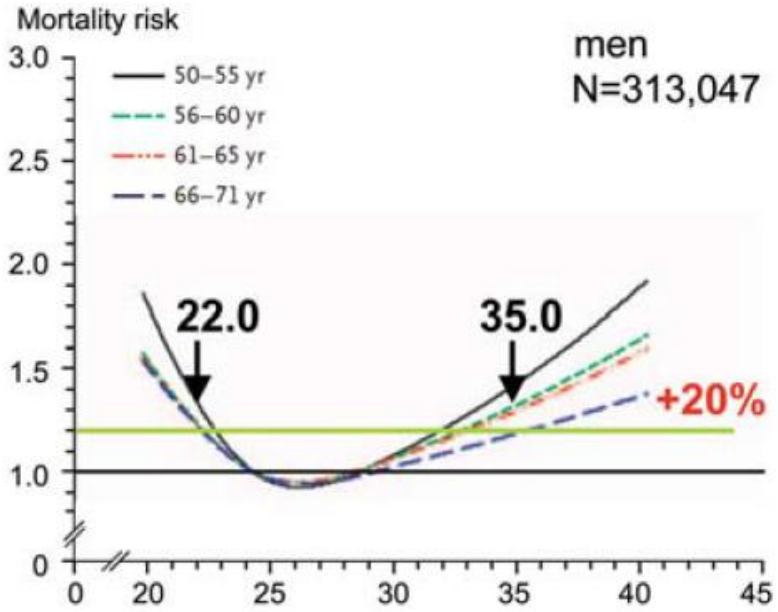
When Thinner Means Sicker
and Heavier Means Healthier

The OBESITY PARADOX

CARL J. LAVIE, MD,
WITH KRISTIN LOBERG

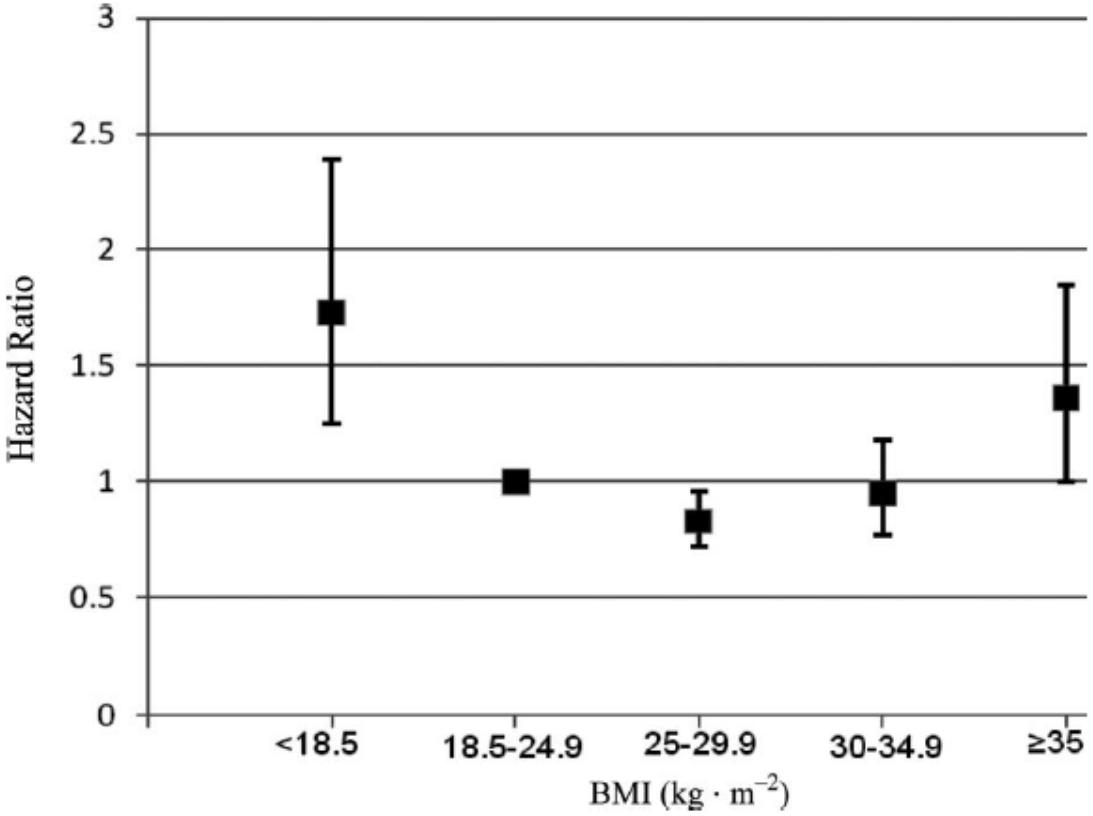
READ BY SEAN PRATT • UNABRIDGED





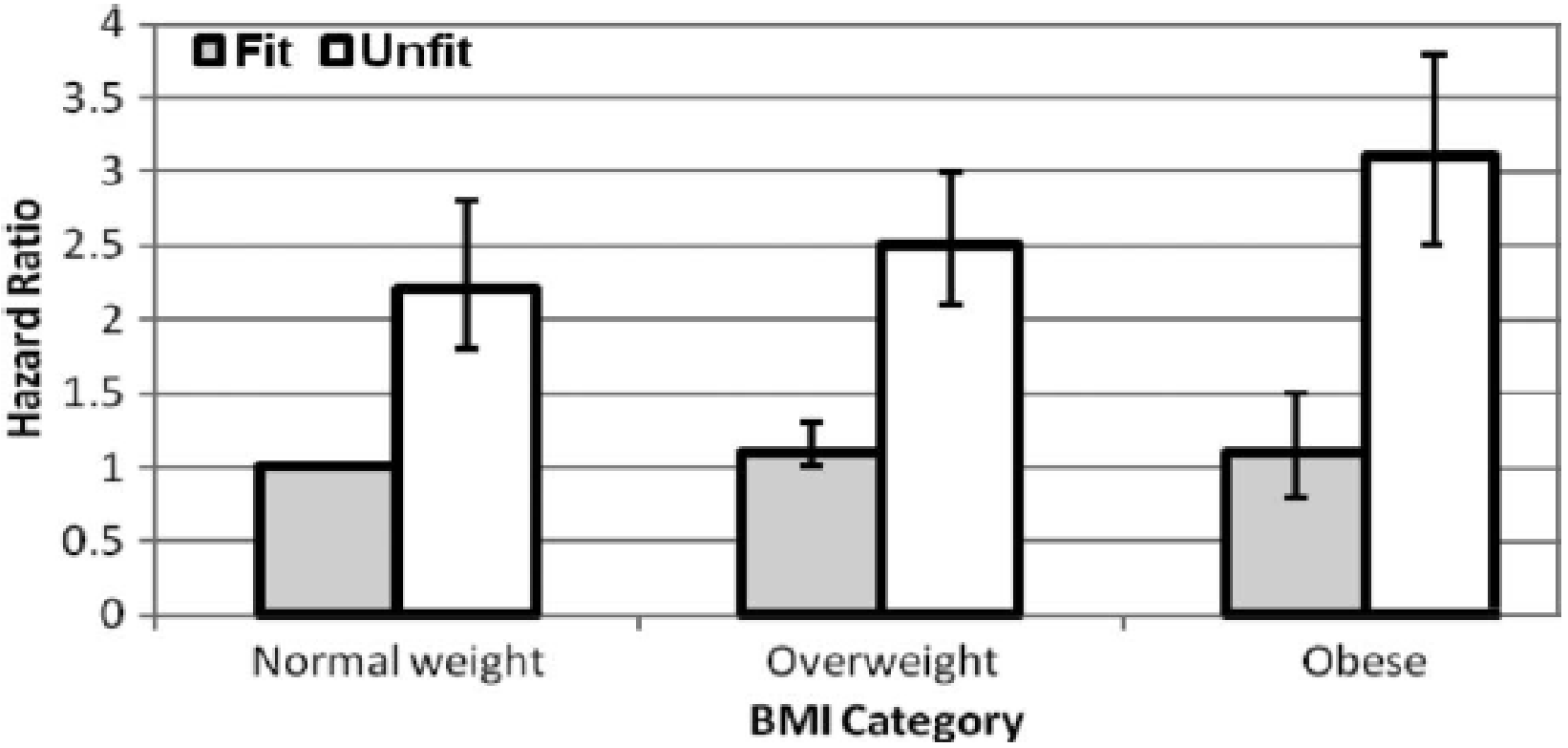
Doehner W, et al. EHJ 2010

CRF è il fattore che «normalizza»



Adjusted for age, smoking status, physical activity frequency, and alcohol consumption, with the relative risk of normal weight (BMI 18.5–24.9 kg m72) set at 1.0.

McAuley PA, and Blair SN, J Sports Sci 2011



McAuley PA, and Blair SN, J Sports Sci 2011

Cholesterol Paradox

Cholesterol paradox: a correlate does not a surrogate make

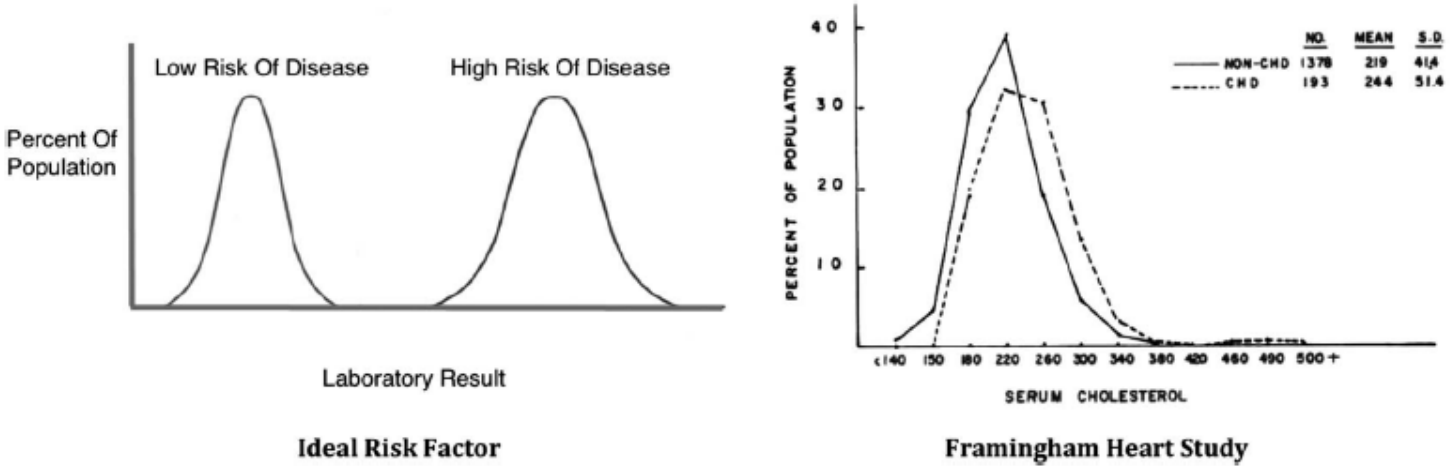


Figure 1 Comparison of ideal risk factor with Framingham Heart Study cholesterol distribution in patients who developed coronary heart disease (CHD) and those that did not develop coronary heart disease (NON-CHD).[3] Cholesterol values are mg/dL. Reprinted with permission of the publisher.

Esempi di studi randomizzati controllati da cui **non emerge una riduzione della mortalità** in relazione all'abbassamento del colesterolo…

CHOLESTEROL PARADOX?

Table 1 Examples of cholesterol lowering randomised controlled trials that reported no mortality benefit

Study	Patient population size and characteristics	Intervention	Mean duration	Cholesterol reduction	CVD event reduction
A to Z	4497 ACS	Simvastatin 0–20 mg/day or simvastatin 40–80 mg/day	6–24 months	19% LDL	No (HR 0.89, 95% CI 0.76 to 1.04)
ACCELERATE	12 092 high risk	Evacetrapib 130 mg/day	30 months	37% LDL	No (HR 1.01, 95% CI 0.91-1.12)
AIM-HIGH	3414 CVD, low HDL, on simvastatin ±ezetimibe	Niacin ER 1.5–2.0 g/day	3 years	16% LDL	No (HR 1.02, 95% CI 0.87 to 1.21)
ALERT	2102 s/p renal transplantation	Fluvastatin 40 mg/day	5.1 years	32% LDL	No (RR 0.83, 95% CI 0.64 to 1.06)
ALLHAT-LLT	10 355 >55 years, HBP, moderate hypercholesterolaemia	Pravastatin 40 mg/day	4.8 years	28% LDL	No (RR 0.91, 95% CI 0.79 to 1.04)
ASCOT-LLA	10 305 HBP, low-average cholesterol	Atorvastatin 10 mg/day	3.3 years	29% LDL	Yes (HR 0.64, 95% CI 0.50 to 0.83)
ASPEN	2410 T2DM	Atorvastatin 10 mg/day	4 years	29% LDL	No (HR 0.9, 95% CI 0.73 to 1.12)
AURORA	2776 haemodialysis	Rosuvastatin 10 mg/day	3.8 years	43% LDL	No (HR 0.96, 95% CI 0.84 to 1.11)
CARDS	2838 T2DM	Atorvastatin 10 mg/day	3.9 years	40% LDL	Yes (RInR 37%, 95% CI 17% to 52%)
CARE	4149 s/p MI, average cholesterol	Pravastatin 40 mg/day	5 years	28% LDL	Yes (RInR 24%, 95% CI 9% to 36%)
CDP	8341 men s/p MI	Dextrothyroxine 6 mg/day	3 years	11% TC	No (excess mortality, premature trial termination)
CDP	8341 men s/p MI	Clofibrate 1.8 gm/day	5 years	6% TC	No (Z=1.99)
CDP	8341 men s/p MI	Niacin 3 gm/day	5 years	11% TC	No (Z=−1.49)
CDP	8341 men s/p MI	Oestrogen 2.5 mg/day	56 months	NR	No (excess DVT, PE and cancer, premature trial termination)
CDP	8341 men s/p MI	Oestrogen 5.0 mg/day	18 months	NR	No (excess non-fatal MI, premature trial termination)
CORONA	5011 > 60 years, ischaemic systolic HF	Rosuvastatin 10 mg/day	33 months	45% LDL	No (HR 0.92, 95% CI 0.83 to 1.02)
ENHANCE	720 FH on simvastatin	Ezetimibe 10 mg/day	2 years	16% LDL	No (trend towards excess CVD events)
FIELD	9795 T2DM	Fenofibrate 200 mg/day	6 years	12% LDL	No (HR 0.89, 95% CI 0.75 to 1.05)
GISSI-HF	4574 Chronic HF (40% ischaemic)	Rosuvastatin 10 mg/day	3.9 years	27–32% LDL	No (HR 1.02, 99% CI 0.92 to 1.13)
GISSI-P	4271 Recent MI	Pravastatin 10–40 mg/day	2 years	15% LDL	No (HR 0.90, 95% CI 0.71 to 1.15)
HERS	2763 women with CVD, intact uterus	CEE 0.625 mg+MPA 2.5 mg/day	4.1 years	11% LDL	No (HR 0.99, 95% CI 0.80–1.11, excess morbidity, premature trial termination)
HOPE-3	12 705 HBP, intermediate risk	Rosuvastatin 10 mg/day	5.6 years	26% LDL	Yes (HR 0.76, 95% CI 0.64 to 0.91)
Howard 2006	48 835 postmenopausal women	Low-fat diet	8.1 years	7% LDL	No (HR 0.97, 95% CI 0.90 to 1.06)
HPS2-THRIVE	25 673 vascular disease on statins	Niacin ER 2 gm/d+laropiprant 40 mg/day	3.9 years	16% LDL	No (RR 0.96, 95% CI 0.90 to 1.03)
IDEAL	8888 s/p MI	Atorvastatin 80 mg/day or simvastatin 20 mg/day	4.8 years	20% LDL	No (HR 0.89, 95% CI 0.78 to 1.01)
IMPROVE-IT	18 144 s/p ACS on simvastatin 40 mg/d	Ezetimibe 10 mg/day	6 years	24% LDL	Yes (HR 0.94, 95% CI 0.89 to 0.99)
JUPITER	17 800 LDL <130 mg/dL, hsCRP >2 mg/L	Rosuvastatin 20 mg/day	1.9 years	49% LDL	Yes (HR 0.56, 95% CI 0.46 to 0.69)
MEGA	7932 hypercholesterolaemia	Pravastatin 10–20 mg/day	5.3 years	15% LDL	Yes (HR 0.67, 95% CI 0.49 to 0.91)
Minnesota Coronary Experiment	9423 nursing home and mental hospital residents	PUFA or SFA diet	41–56 months	12.8% TC	No (excess mortality HR 1.22, 95% CI 1.14 to 1.32; excess CVD RR 1.9, 95% CI 1.01 to 3.72)
LIPS	1677 s/p first PCI	Fluvastatin 80 mg/day	3.9 years	27% LDL	Yes (HR 0.78, 95% CI 0.64 to 0.95)
LRC-CPPT	3806 men, hypercholesterolaemia	Cholestyramine	7.4 years	13% LDL	Yes (RInR 19% p<0.05)
Post-CABG	1351 s/p CABG	Lovastatin 2.5–40 mg ± cholestyramine/day	4.3 years	24–25% LDL	No
PREVEND-IT	864 microalbuminuria	Pravastatin 40 mg/day	3.8 years	21% LDL	No (HR 0.87, 95% CI 0.49 to 1.57)
PROSPER	5804 elderly at risk of vascular disease	Pravastatin 40 mg/day	3.2 years	34% LDL	Yes (HR 0.85, 95% CI 0.74 to 0.97)
PROVE-IT	4162 ACS, TC <240 mg/dL	Pravastatin 40 mg/day or atorvastatin 80 mg/day	24 months	35% LDL	Yes (RInR 16%, 95% CI 5% to 26%)
SEAS	1873 mild-moderate aortic stenosis	Simvastatin 40 mg+ezetimibe 10 mg/day	4.4 years	50% LDL	No (HR 0.96, 95% CI 0.83 to 1.12)
SHARP	9270 CKD	Simvastatin 20 mg/day+ezetimibe 10 mg/day	4.9 years	31% LDL	Yes (RR 0.83, 95% CI 0.74 to 0.94)

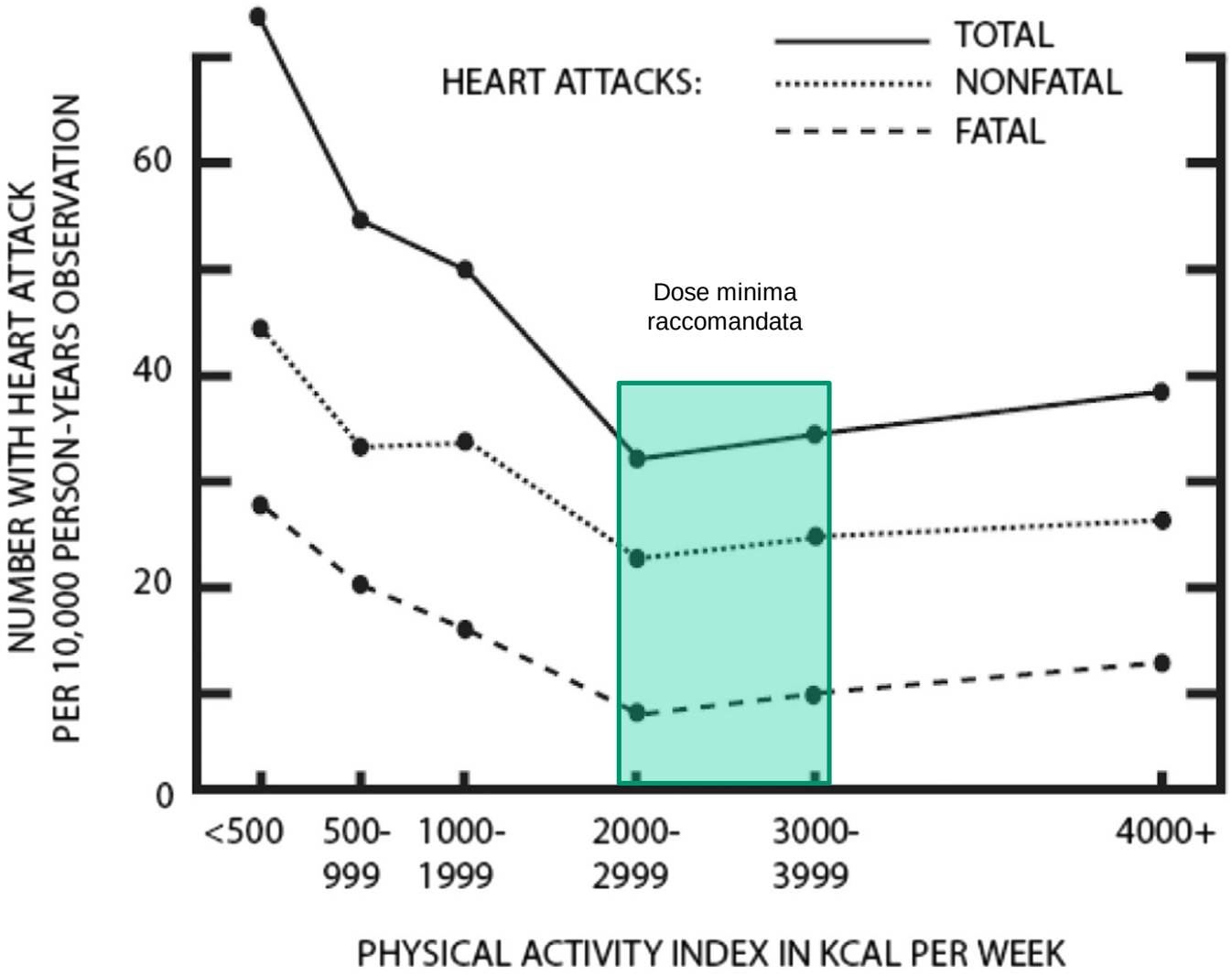
DuBroff R. EBIMED 2016

Table 1 Continued

Study	Patient population size and characteristics	Intervention	Mean duration	Cholesterol reduction	CVD event reduction
St Francis Heart	1005 CCS >80th centile, asymptomatic	Atrovastatin 20 mg/day	4.3 years	39–43% LDL	No (p=0.08)
Sydney Diet Heart Study	458 men s/p recent coronary event	PUFA or SFA diet	39 months	7.8% TC	No (excess mortality p=0.05; excess CVD HR 1.7, 95% CI 1.03 to 2.80)
TNT	10 001 CHD, LDL <130 mg/dL	Atorvastatin 10 mg/day or 80 mg/day	4.9 years	24% LDL	Yes (HR 0.78, 95% CI 0.69 to 0.89)
WHI	10 739 women s/p hysterectomy	CEE 0.625 mg/day	6.8 years	13% LDL	No (HR 1.12, 95% CI 1.01 to 1.24; excess stroke, premature trial termination)
WHO	15 745 men, high cholesterol	Clofibrate 1.6 gm/day	5.3 years	9% TC	No (mortality increased 25%)
WOSCOPS	6595 men, hypercholesterolaemia	Pravastatin 40 mg/day	4.9 years	26% LDL	Yes (RinR 31%, 95% CI 17% to 43%)
4D	1255 T2DM, haemodialysis	Atrovastatin 20 mg/day	4 years	42% LDL	No (HR 0.92, 95% CI 0.77 to 1.10)

ACS, acute coronary syndrome; CABG, coronary artery bypass graft surgery; CCS, coronary calcium score; CEE, conjugated equine oestrogen; CHD, coronary heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DVT, deep venous thrombophlebitis; ER, extended release; FH, familial hypercholesterolaemia; HBP, high blood pressure; HDL, high-density lipoprotein cholesterol; HF, heart failure; hsCRP, highly sensitive C reactive protein; LDL, low-density lipoprotein cholesterol; MI, myocardial infarction; NR, not reported; MPA, medroxyprogesterone acetate; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PE, pulmonary embolus; PUFA, polyunsaturated fatty acid; RR, rate ratio; RinR, reduction in risk; SFA, saturated fatty acid; TC, total cholesterol; T2DM, type 2 diabetes mellitus.

Exercise Paradox



Paffenbarger RS, et al. Am J Epidemiol 1978

Editorials

THE PARADOX OF EXERCISE

The NEW ENGLAND JOURNAL of MEDICINE

· November 9, 2000

BARRY J. MARON, M.D.

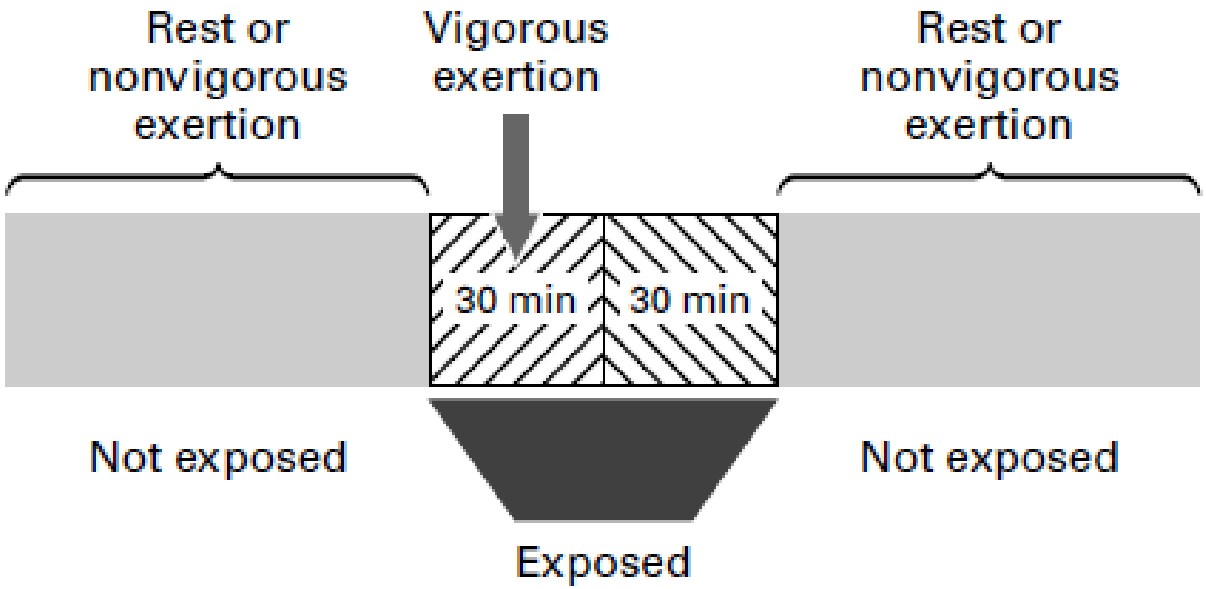
Minneapolis Heart Institute Foundation
Minneapolis, MN 55407

TRIGGERING OF SUDDEN DEATH FROM CARDIAC CAUSES BY VIGOROUS EXERTION

CHRISTINE M. ALBERT, M.D., M.P.H., MURRAY A. MITTLEMAN, M.D., DR.P.H., CLAUDIA U. CHAE, M.D., M.P.H, I.-MIN LEE, M.B., B.S., SC.D., CHARLES H. HENNEKENS, M.D., DR.P.H., AND JOANN E. MANSON, M.D., DR.P.H.

The NEW ENGLAND JOURNAL of MEDICINE

Volume 343 Number 19 · 1355



Albert CM, et al NEJM 2000

TABLE 2. EFFECT OF HABITUAL VIGOROUS EXERCISE ON THE RISK OF SUDDEN DEATH DURING VIGOROUS EXERTION.

FREQUENCY OF HABITUAL VIGOROUS EXERCISE	SUDDEN DEATHS		RELATIVE RISK (95% CI)*
	TOTAL	RELATED TO VIGOROUS EXERTION	
	no.		
<1 time/wk	32	3	74.1 (22.0–249)
1–4 times/wk	67	13	18.9 (10.2–35.1)
≥5 times/wk	23	7	10.9 (4.5–26.2)

*The relative risk is the risk of sudden death during and 30 minutes after an episode of vigorous exertion, as compared with the risk during periods of lighter exertion or none. CI denotes confidence interval.

Albert CM, et al NEJM 2000

- Therefore, the effects of exercise with respect to the potentially devastating consequences of coronary artery disease are complex and contradictory.
- The benefits do not come without some risk, **particularly** when **vigorous exertion** is undertaken abruptly **by untrained or previously sedentary persons.**
- Nevertheless, given the substantial and compelling data from both prospective and retrospective studies, **it is reasonable to conclude that the hazards of physical activity are outweighed by the overall cardiovascular benefits of exercise.**
- The balance of the evidence thus supports the value and importance of participation in regular exercise regimens.

Maron BJ. NEJM 2000

Evidenze epidemiologiche osservazionali

ATTIVITA' FISICA E SALUTE: RELAZIONE DOSE-RISPOSTA?

I-Min Lee, MD, ScD, modificato

Trial clinici vs. Studi Osservazionali

- **“The paradox of the clinical trial is that it is the best way to assess whether an intervention works, but is arguably the worst way to assess who will benefit from it.”**
- **“It must be recognised explicitly that, in order to apply the results of the trials to individual patients, there must be a parallel investment in observational studies – both quantitative and qualitative.”**

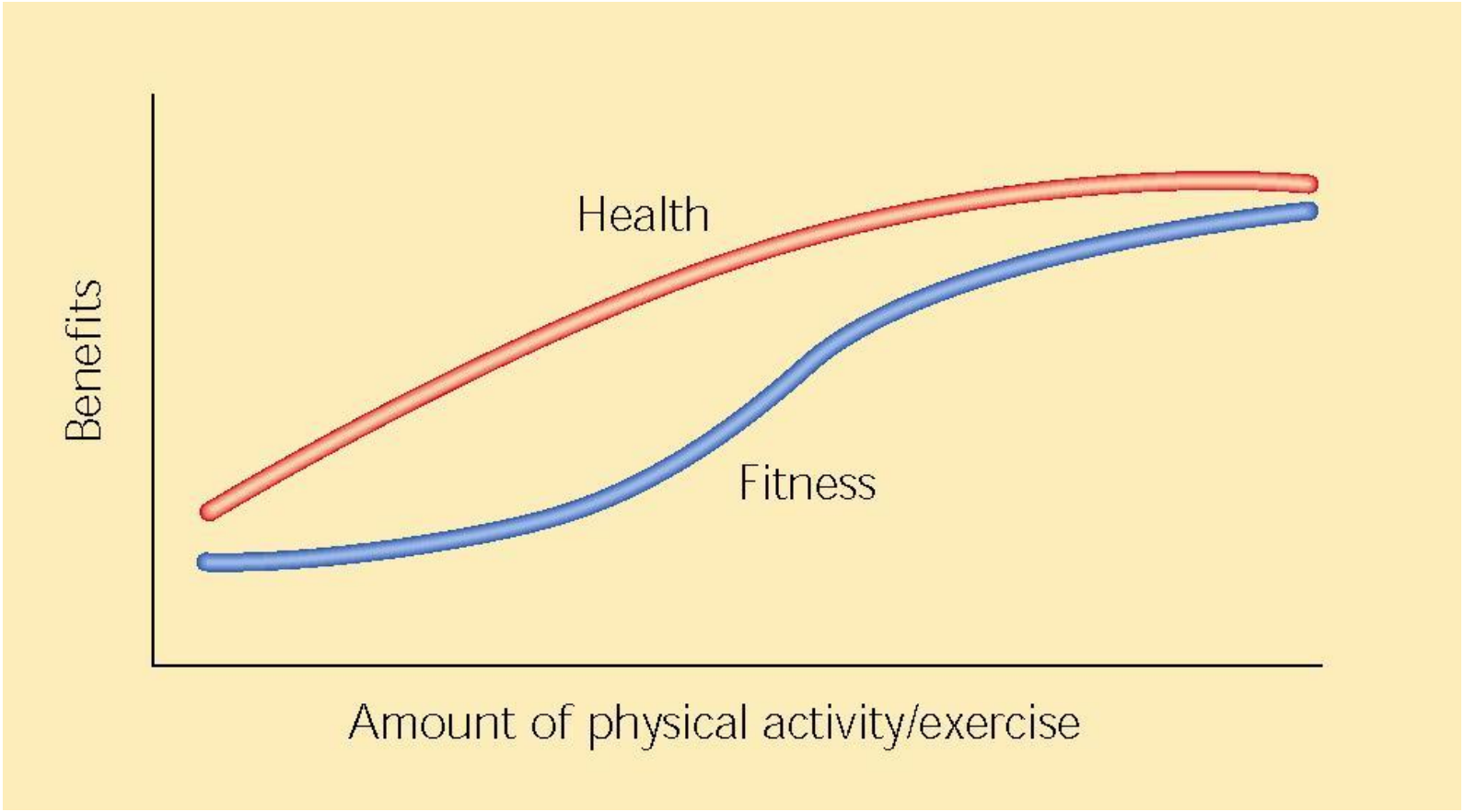
Mant; Lancet 1999

- **Anni ’50-’90**
- **Anni ‘90 in poi**

- **L’attività fisica riduce il rischio di malattie croniche non trasmissibili?**
- **Si, l’attività fisica protegge…**

- **Esiste una relazione ‘Dose-risposta’?**
  - Quanto forte?
  - Quanto a lungo?
  - Quante volte?
  - Quanto recupero?

How much is enough?



Dose-Risposta: Definizione

- “Describes the change in effect … caused by differing levels of exposure to a stressor”; central to determining safe and hazardous levels for drugs and pollutants (Wikipedia)
- PubMed search for “dose response” and “exercise” – studies as far back as 1967, but mainly related to drug effects; e.g., effect of beta-blocker on exercise tolerance in angina patients
- In the mid-1980’s, we begin to see the term used for the study of different doses of PA
- Influence of medical/epidemiologic principles?

Primi anni 2000

- “Most of the evidence currently available seems to be related to the effects (benefits or risks) of regular physical activity rather than to the relationship between dose and response.”

Dose-Response Issues Concerning PA and Health: An Evidence-Based Symposium
(Hockley Valley, Canada, 2000)

2005-2010

- **“Participation in aerobic and muscle-strengthening physical activities above minimum recommended amounts provides additional health benefits ...” (DI PIU’ SEMBRA MEGLIO)**
- **It is well-documented that PA of longer duration or higher intensity is associated with additional risk decrements but the exact shape of the … curve remains unclear and may vary depending on the health outcome of interest and baseline PA level …”**

Physical activity and public health: Updated recommendation for adults from ACSM/AHA. Haskell W, et al, MSSE 2007

Perché è interessante la “risposta alla dose”?

- **Knowledge is useful in clinical and public health setting**
- **Dose-response is one criterion used to judge cause-and-effect relation in observational studies**
- **Dose-response can help us understand the biology underlying physical activity-disease relation**

Limiti metodologici

Componente	Variabile
Modo di esercizio	Occupazionale Ricreazionale Sport Cammino Corsa Ciclismo Nuoto etc
Volume di esercizio	Ore settimanali Kcal MET/H/sett MET/min/d etc
Intensità di esercizio	MET Velocità… %FC %VO2max etc
Durata di esercizio	Ore/giorno, ore/sett, frequenza/sett, etc

Limiti metodologici

- **Variabili categoriche…**
- **Variabili continue…**
  - Terzili
  - Quartili
  - Quintili
  - Altri criteri arbitrari (sopra/sotto cut-off arbitrari)
  - Etc.

Limiti metodologici

- **… self-reported…!!! Per quanto «validati» si tratta di questionari auto/etero somminstrati…**
- **Pochi studi con pochi casi in cui l'attività svolta sia stata valutata oggettivamente…**

… self-reported…

- … Although 62% of US adults report meeting recommendations, only 9.6% of adults do so when objective accelerometer data are used …

Heinrich KM, et al. Frontiers in Public Health 2017

Study	Validation Description	Exposure description for this analysis[a]	Death ascertainment
NIH-AARP Diet and Health Study	Has shown expected associations with mortality[1] and risk of breast[2], endometrial [3] and colon cancers[3,4]	Summary variable of moderate and vigorous activities	Death Master File and National Death Index (NDI) showed 87-98% sensitivity[5]
Campaign Against Cancer and Heart Disease (CLUE II)	Derived from the Nurses' Health Study (NHS), which has shown correlations between 0.79-0.83 comparing recall to questionnaires and 0.59-0.62 comparing diaries to questionnaires[6]	Moderate activities: walking, calisthenics and bicycling Vigorous activities: jogging, running, tennis, and swimming	Date and cause of death are ascertained monthly from death certificates, and annually from a state death linkage through an agreement with Maryland DHMH, Vital Statistics, and supplemented with linkage to the NDI. Obituaries are monitored daily[7]
Cancer Prevention Study II (CPS II)	Derived from NHS questionnaire and has shown expected inverse associations with breast[8] and colon[9] cancer risk in this cohort	Moderate activities: walking, dancing, biking, aerobics/ calisthenics Vigorous activities: jogging/running, lap swimming, tennis or racquetball	National Death Index captured 93% of all deaths and 97% where social security numbers were available[10]
U.S. Radiologic Technologists study (USRT)	Has shown expected inverse associations with breast cancer[11]	Moderate activities: walking/hiking for exercise Vigorous activities: aerobics, jogging, swimming	Deaths identified from Social Security Administration records (99.3% available) and causes of death obtained from NDI-Plus (94%) [12]
Women's Health Study (WHS)	Derived from NHS questionnaire and has shown correlations r=0.36 for women <65, 0.35 for women 65-<70, and 0.33 for women ≥70 years old comparing the physical activity questionnaire to vector magnitude accelerometer values [b]	Moderate activities: Walking, bicycling Vigorous activities: jogging, running, aerobics	Validated against medical records and/or National Death Index[13-15]
Women's Lifestyle and Health Study (WLHS)	Has shown expected inverse associations with mortality[16]	Moderate activities: Walking briskly, horseback riding, skiing Vigorous activities: more strenuous activities	Linkage to national registries virtually complete[17]

Arem H. et al. JAMA 2015

Exercise Paradox

33% reduction in all-cause mortality
35% reduction in cardiovascular mortality
32% reduction in hypertension risk
42% reduction in type 2 diabetes risk
Reduced risk of certain cancers
Increase in healthy ageing

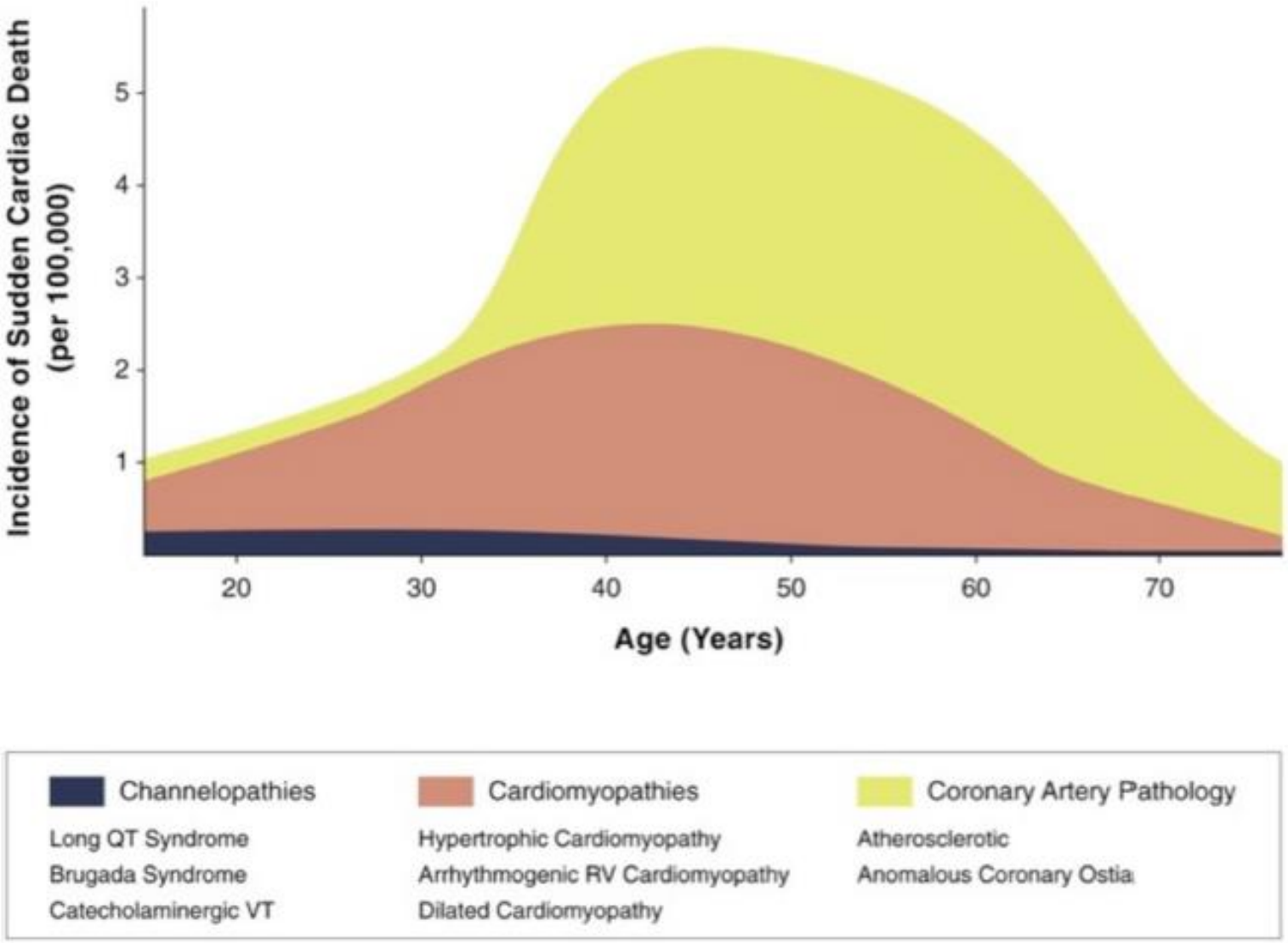
Mature athlete

High lifetime volume of vigorous intensity exercise:
↑Risk of AF
↑Coronary artery calcification
Myocardial fibrosis

Elevated SCD risk
~1:50 000

Positive effects of exercise on health

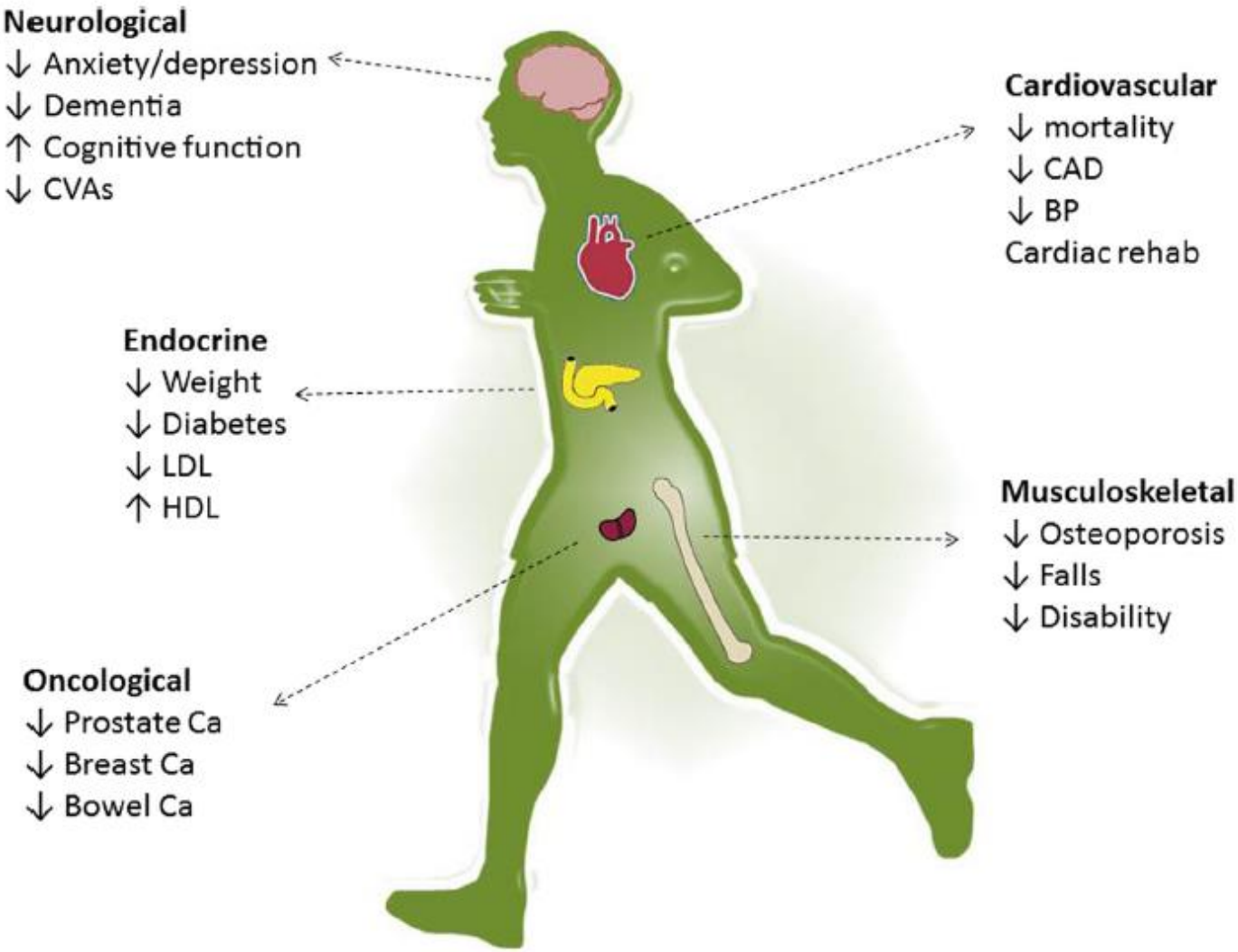
D'Silva A., Sharma S. Heart 2017



D'Silva A., Sharma S. Heart 2017

The U-shaped relationship between exercise and cardiac morbidity

Merghani A. et al. Trends CV Med 2016



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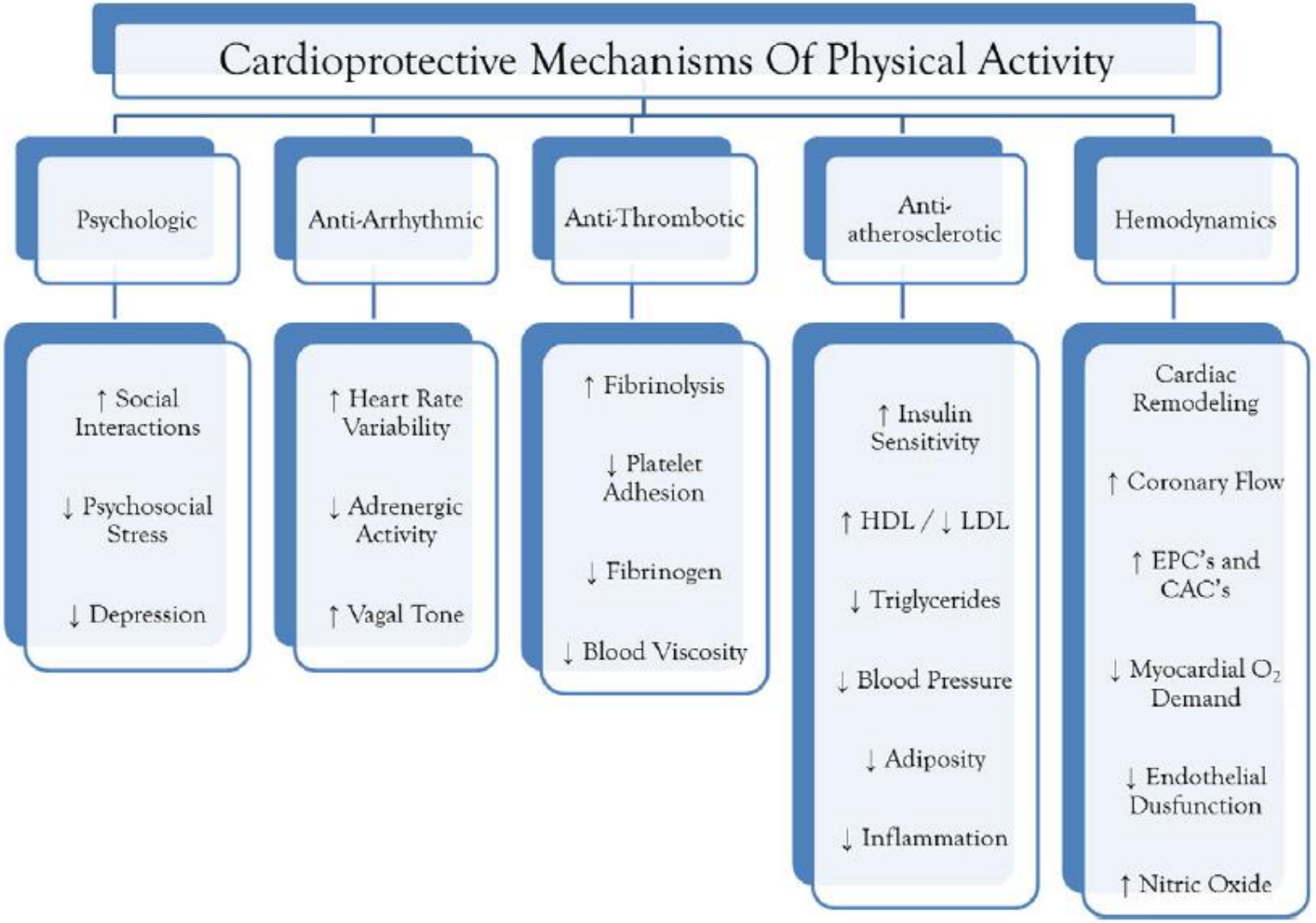
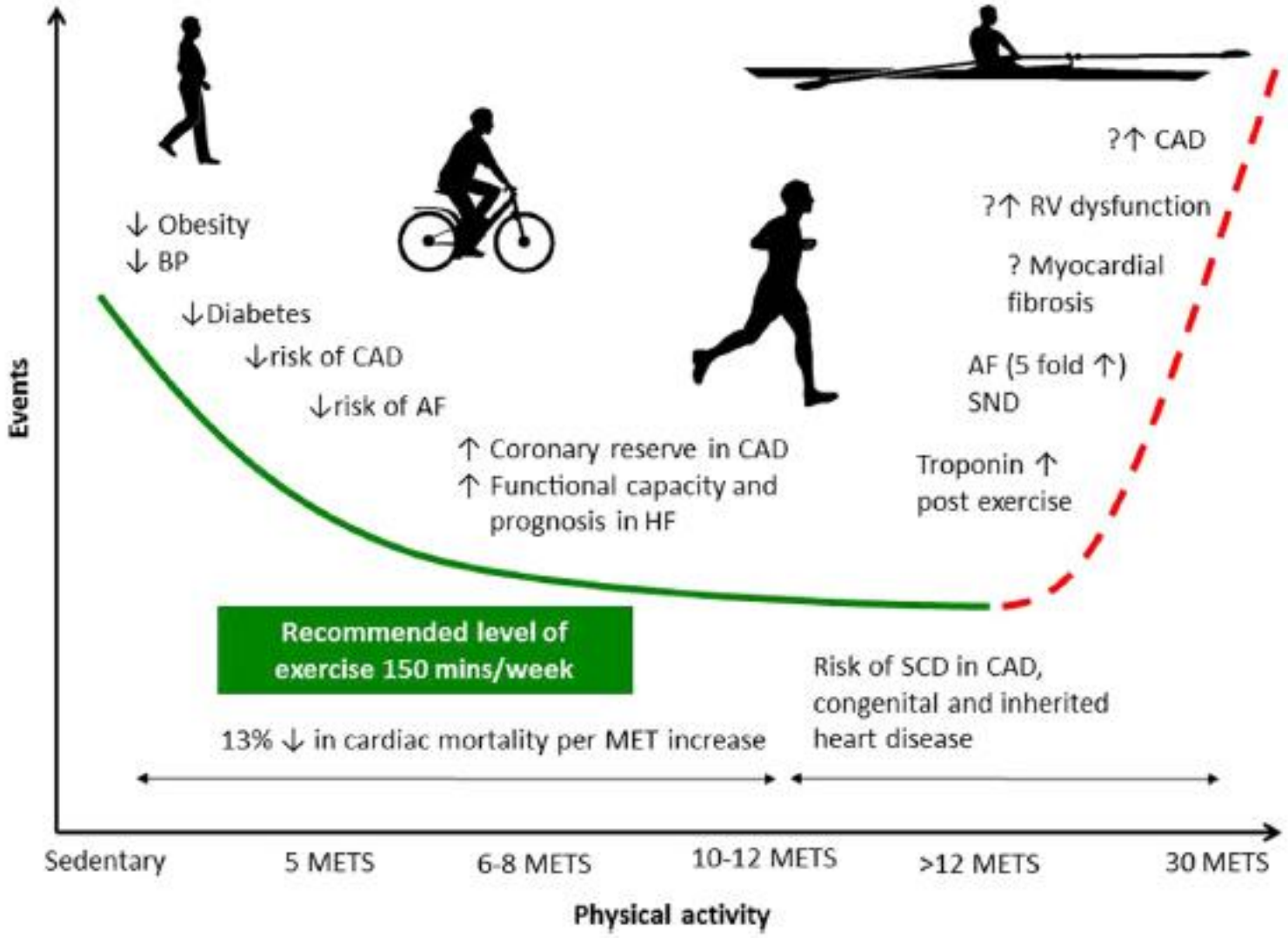


Kachur S, et al. Progr CVD 2017



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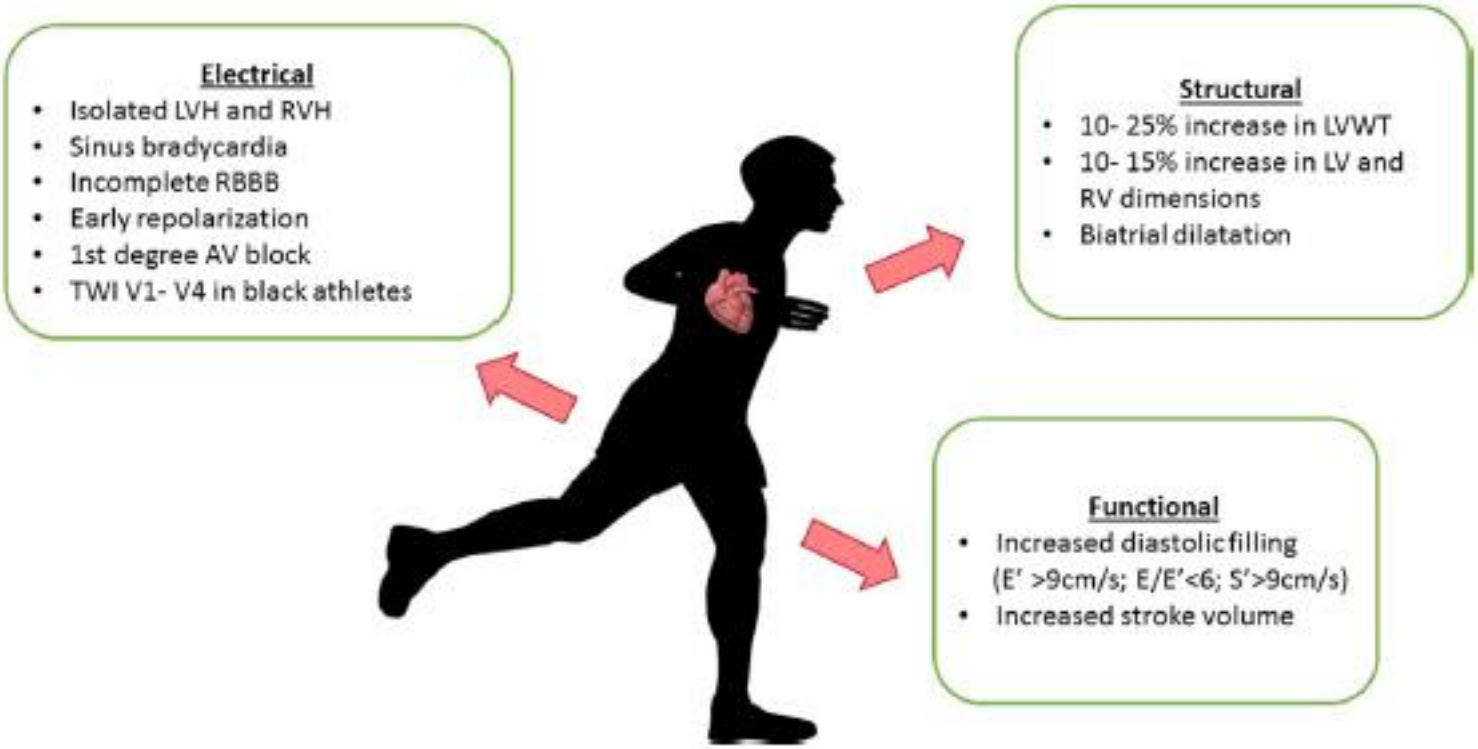

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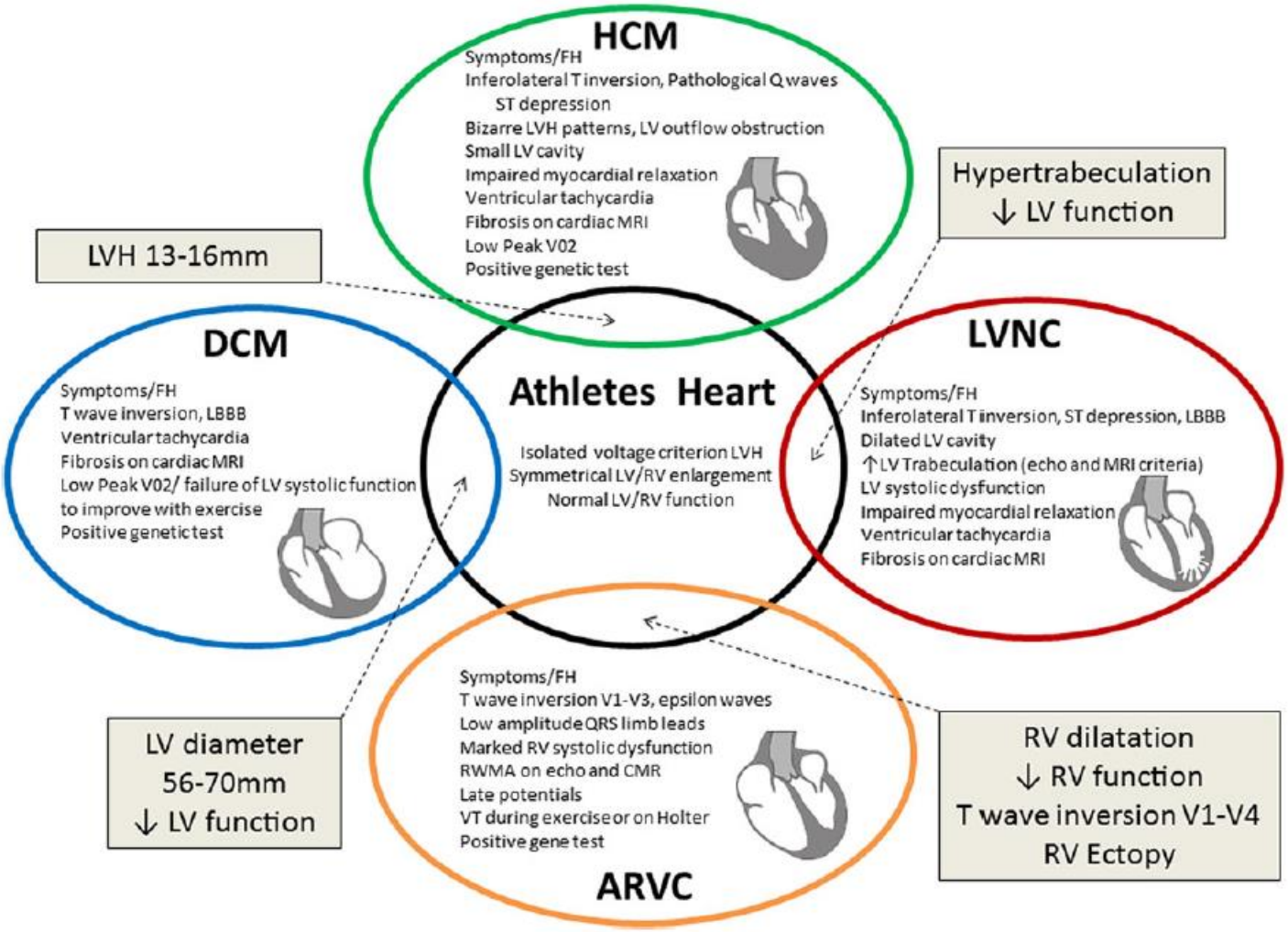
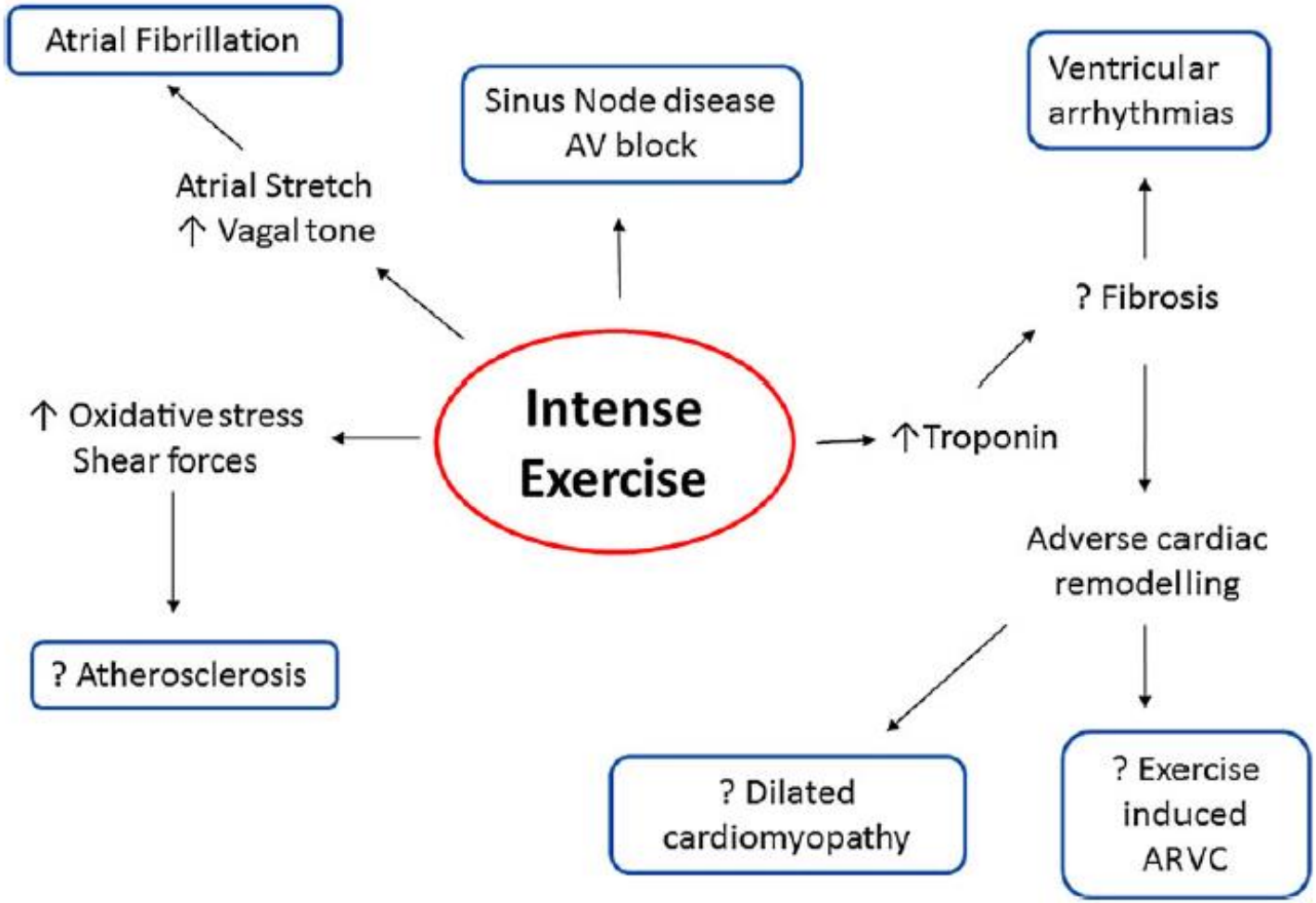
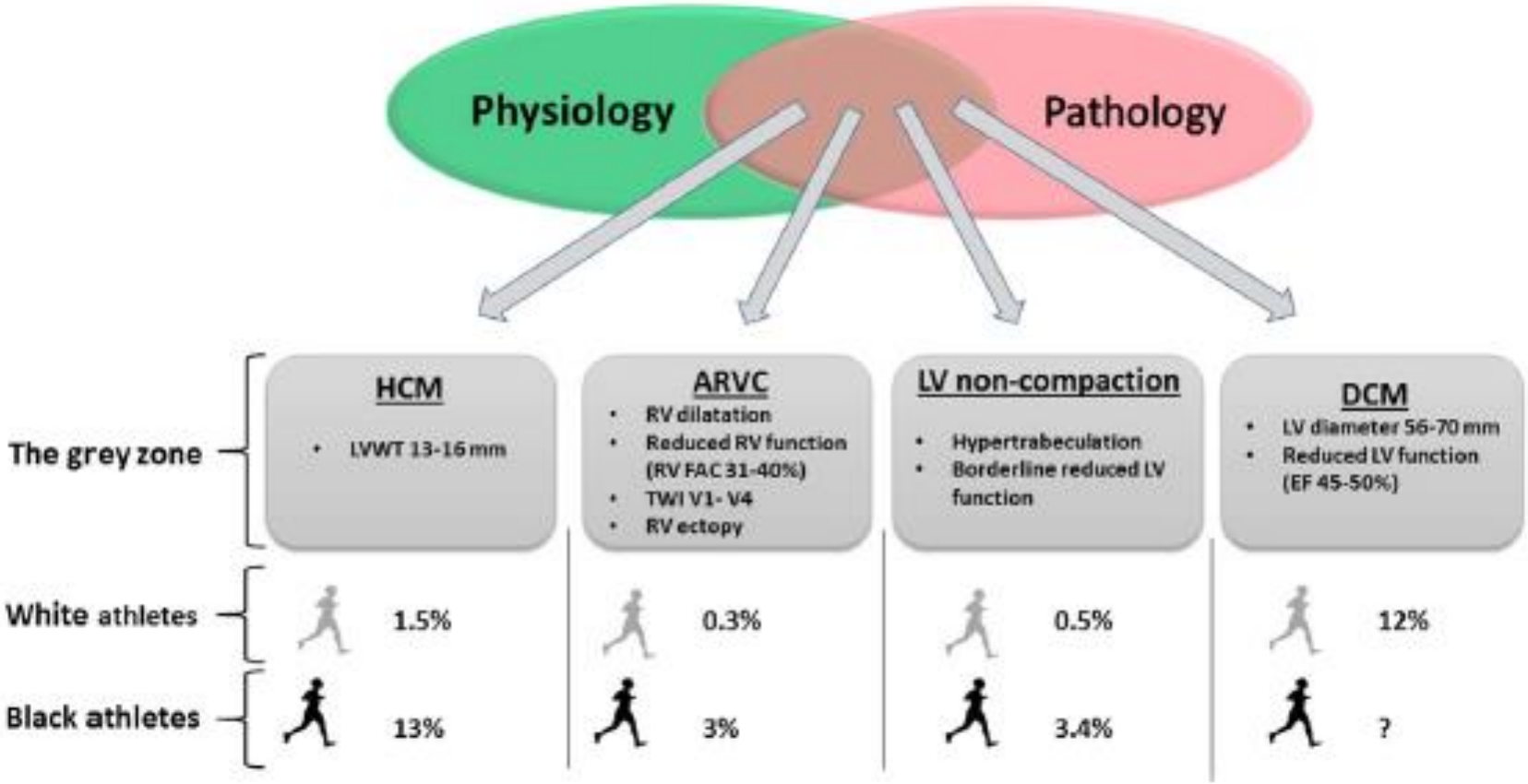


Sharma S. et al. EHJ 2015



Sharma S. et al. EHJ 2015



Merghani A. et al. Trends CV Med 2016

- The prevalence of sudden cardiac death (SCD)among young athletes is not common,ranging from approximately **1 in 50,000 to 1 in 200,000** depending on the athletic population being studied and the methods for data collection [37,38].
- In contrast, SCD in older athletes is predominantly due to atherosclerotic coronary artery disease. Many such individuals have established risk factors for CAD, suggesting that exercise may not confer the same protections from atheroma in the presence of ongoing risk factors.
- Most deaths in sport occur in middle-aged recreational athletes.
- Current strategies to prevent SCD in this cohort rely largely on bystander cardiopulmonaryresuscitation(CPR) and early utilizationof an automated external defibrillator (AED),which is associated with improved outcomes in23–46% [39–41].

Merghani A. et al. Trends CV Med 2016

- […However, a major limiting factor of the study was that more than half of the runners in the study were **previous smokers** and 5% were **active smokers**…]

Merghani A. et al. Trends CV Med 2016

Dose of Jogging and Long-Term Mortality

The Copenhagen City Heart Study

1,098 healthy joggers and 3,950 healthy nonjoggers

Schnohr P. et al. JACC 2015

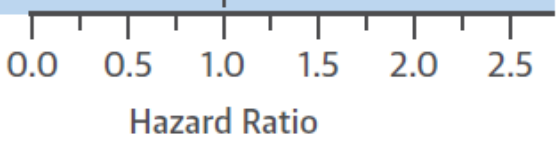
TABLE 1 Joggers Categorized as Light Joggers, Moderate Joggers, or Strenuous Joggers on the Basis of Self-Reported Pace, Quantity, and Frequency of Jogging

	Jogging Pace								
	Slow			Average			Fast		
	<2.5 h/week	2.5–4 h/week	>4 h/week	<2.5 h/week	2.5–4 h/week	>4 h/week	<2.5 h/week	2.5–4 h/week	>4 h/week
Frequency of jogging									
≤3 times/week	Light	Moderate	Moderate	Light	Moderate	Moderate	Moderate	Moderate	Strenuous
>3 times/week	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Strenuous	Strenuous

Light: 5 mph
Average: 5-7 mph
Fast: > 7mph

Schnohr P. et al. JACC 2015

DOSE OF JOGGING	NO. OF PARTICIPANTS	ALL-CAUSE MORTALITY DEATHS	FOREST PLOT
Adjusted for age and sex			
Sedentary nonjogger (reference)	413	128	
Light jogger	576	7	
Moderate jogger	262	8	
Strenuous jogger	40	2	3.67
Adjusted for age, sex, smoking, alcohol intake, education, and diabetes			
Sedentary nonjogger (reference)	394	120	
Light jogger	570	7	
Moderate jogger	252	8	
Strenuous jogger	36	2	8.14

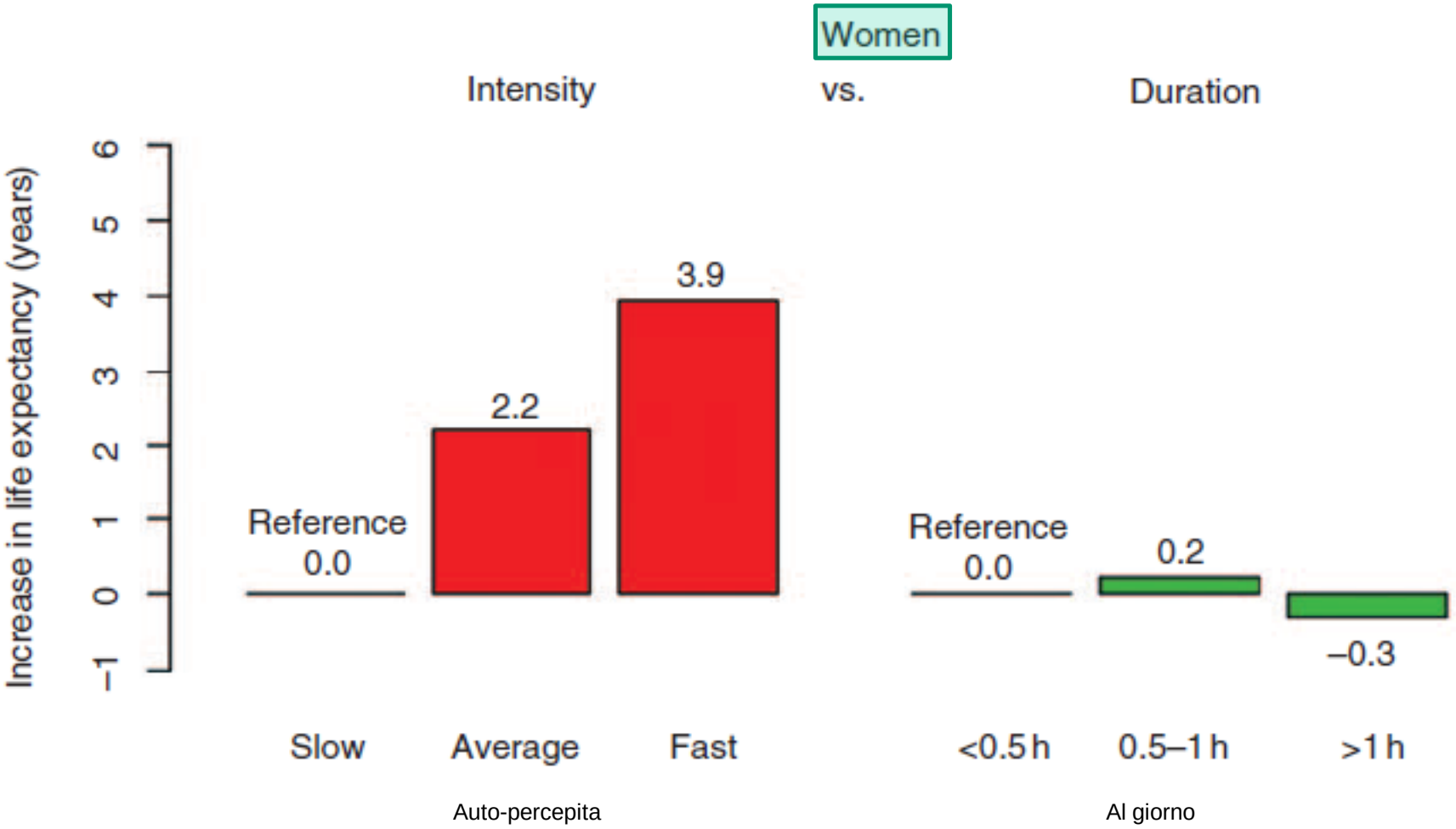


Schnohr P. et al. JACC 2015

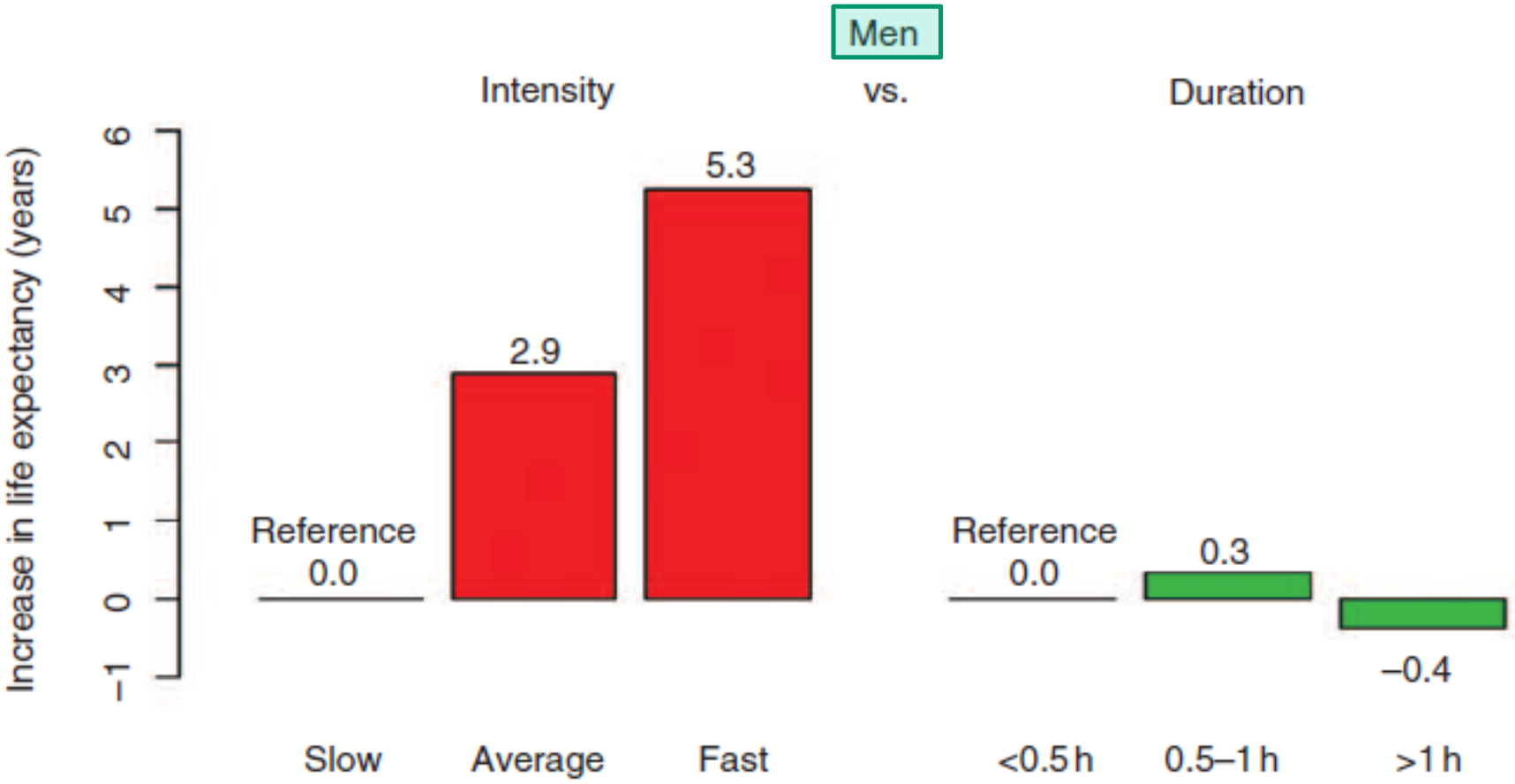
Intensity versus duration of cycling, impact on all-cause and coronary heart disease mortality: the Copenhagen City Heart Study

5106 apparently healthy men and women aged 21–90

Schnohr P. et al. EJPC 2011



Schnohr P. et al. EJPC 2011



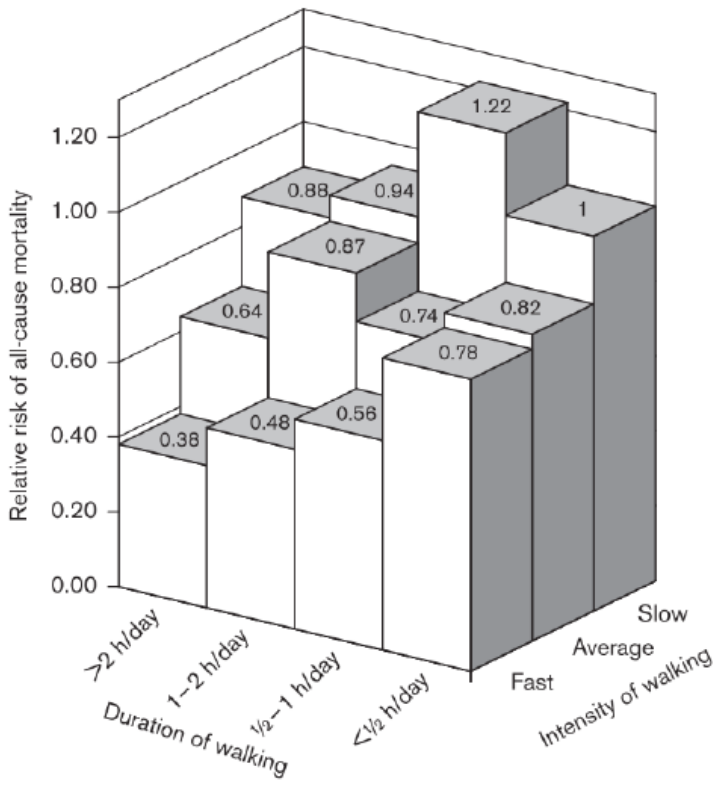
Schnohr P. et al. EJPC 2011

Intensity versus duration of walking, impact on mortality: the Copenhagen City Heart Study

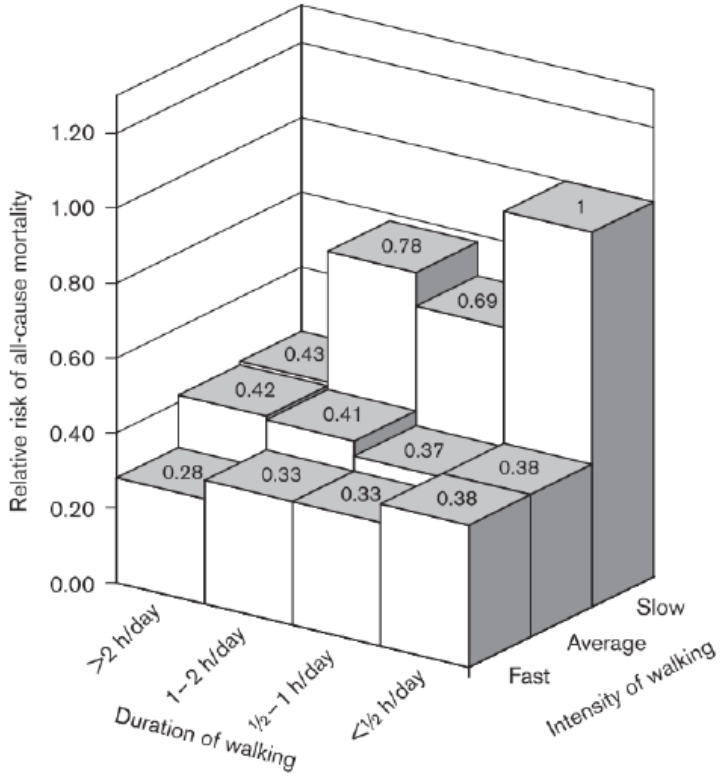
7308 healthy women and men aged 20–93

Schnohr P. et al. EJPC 2007

Women



Men

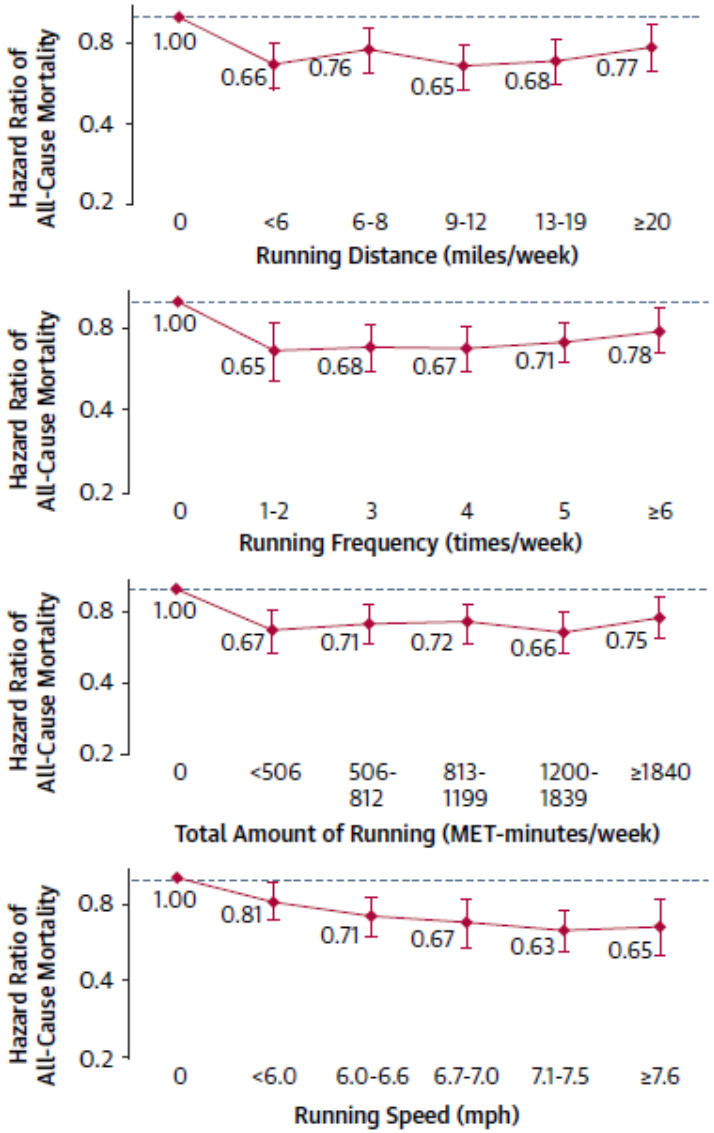


Schnohr P. et al. EJPC 2007

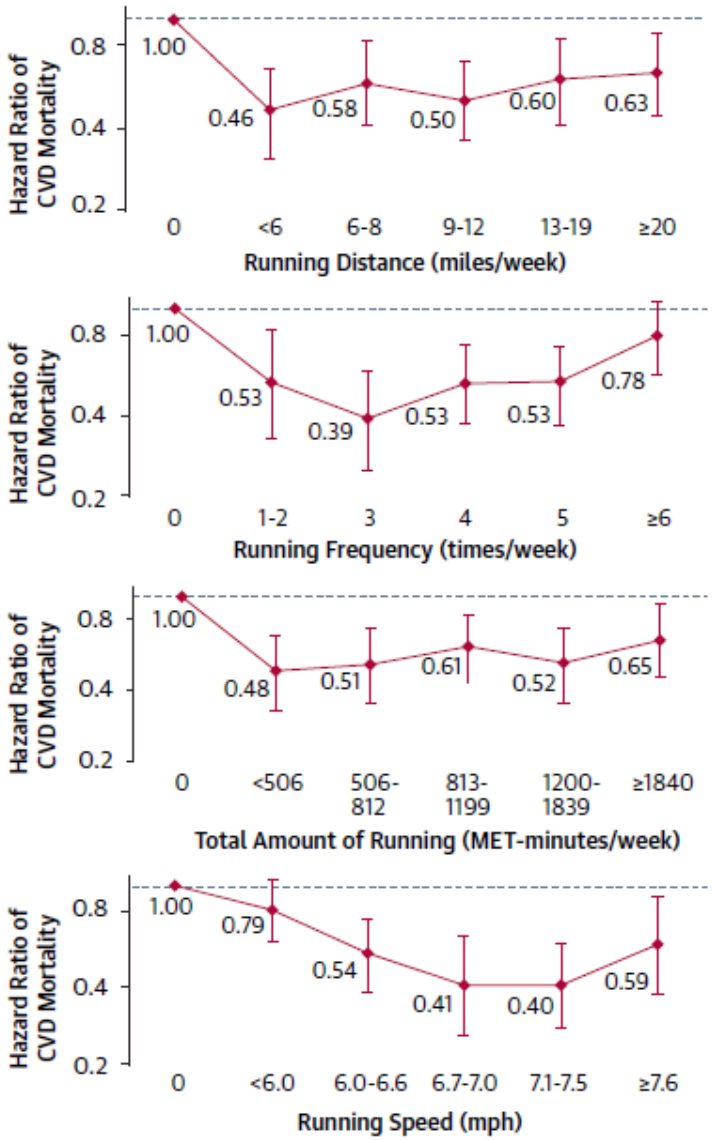
Leisure-Time Running Reduces All-Cause and Cardiovascular Mortality Risk

In 55,137 adults, 18 to 100 years of age (mean age 44 years).

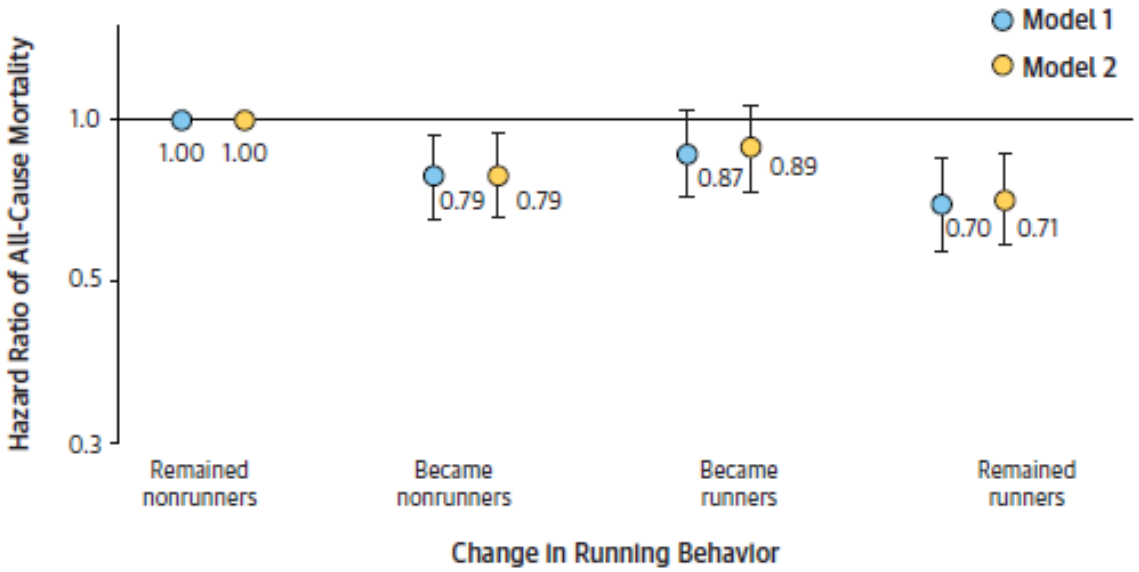
Lee D-C. et al. JACC 2014

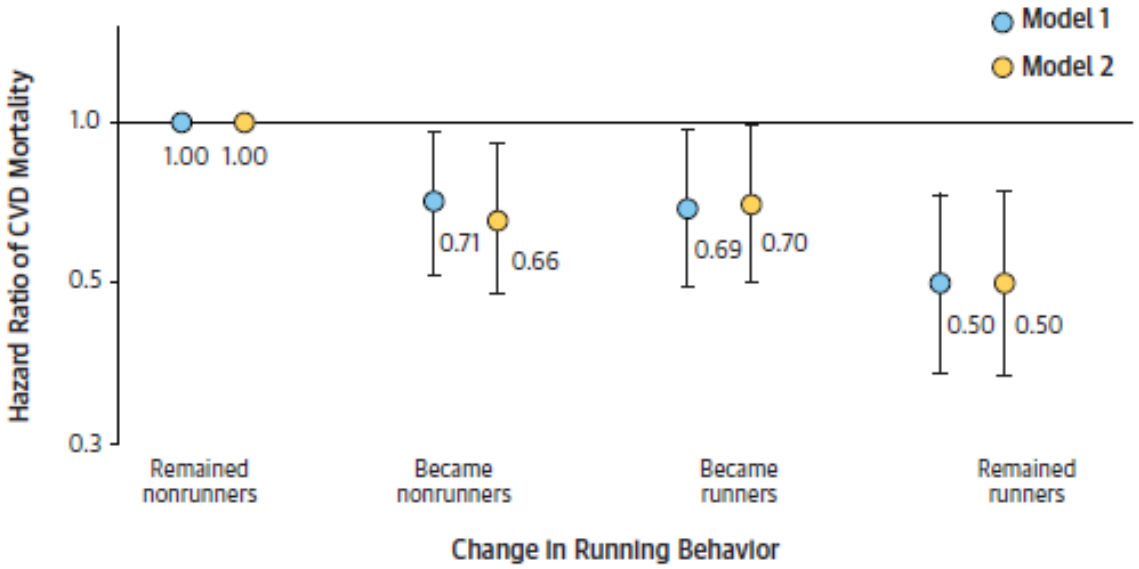


Lee D-C. et al. JACC 2014

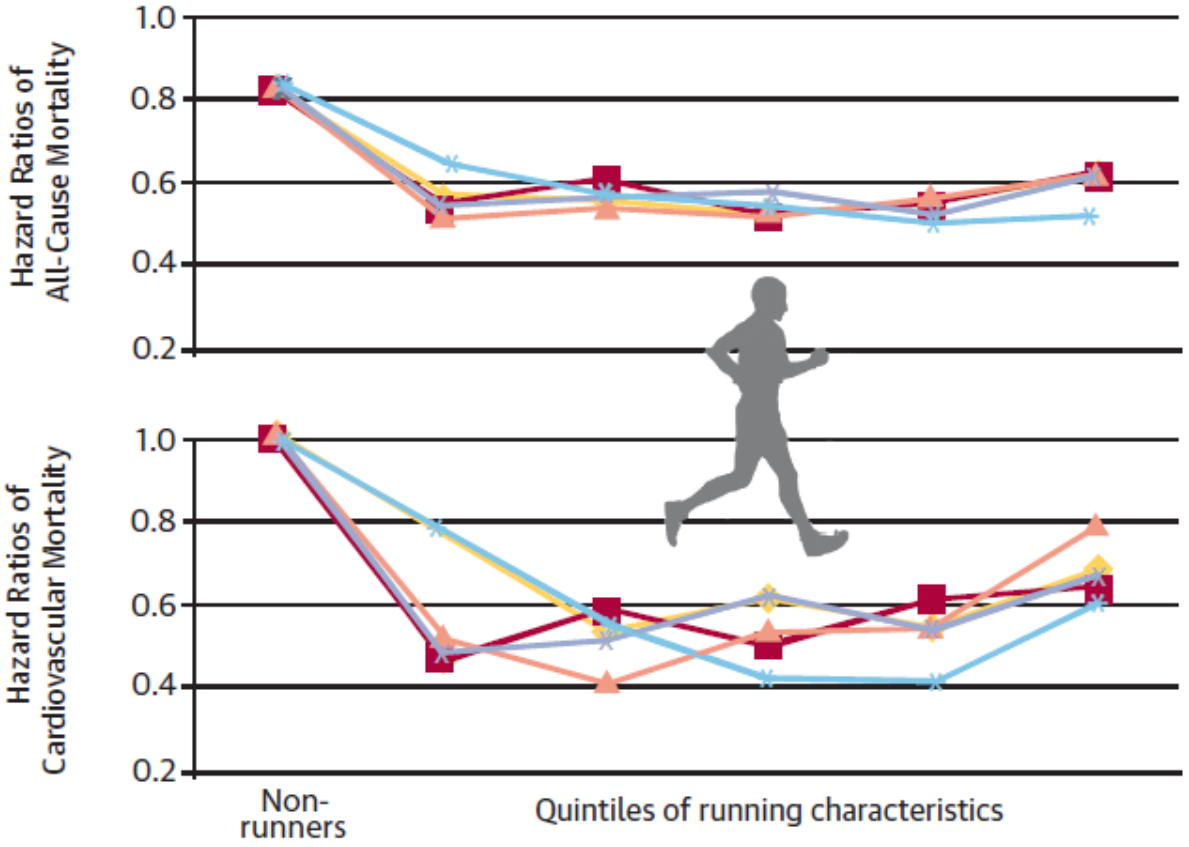


Lee D-C. et al. JACC 2014



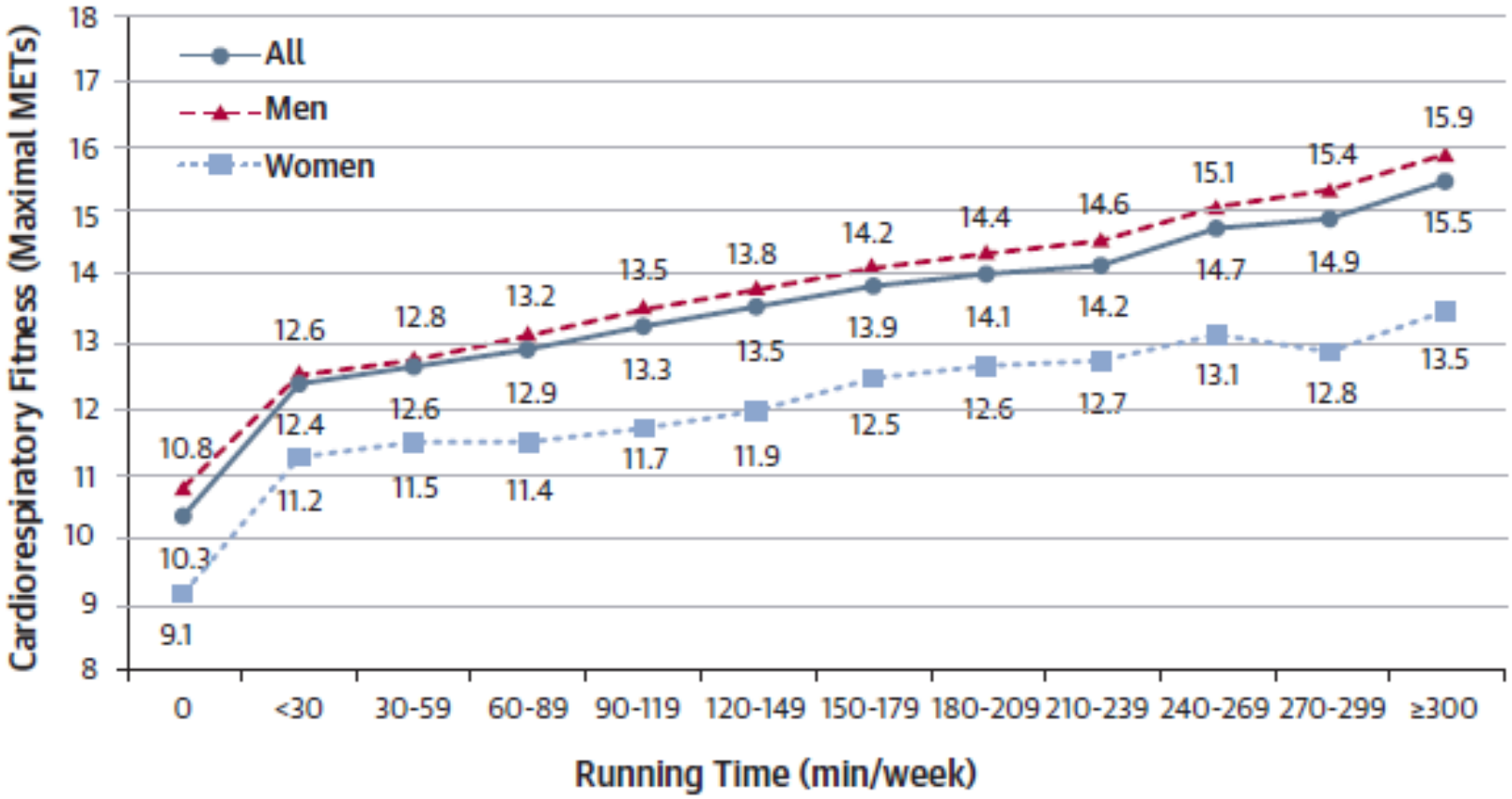


Lee D-C. et al. JACC 2014



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

Lee D-C. et al. JACC 2014



Lee D-C. et al. JACC 2014

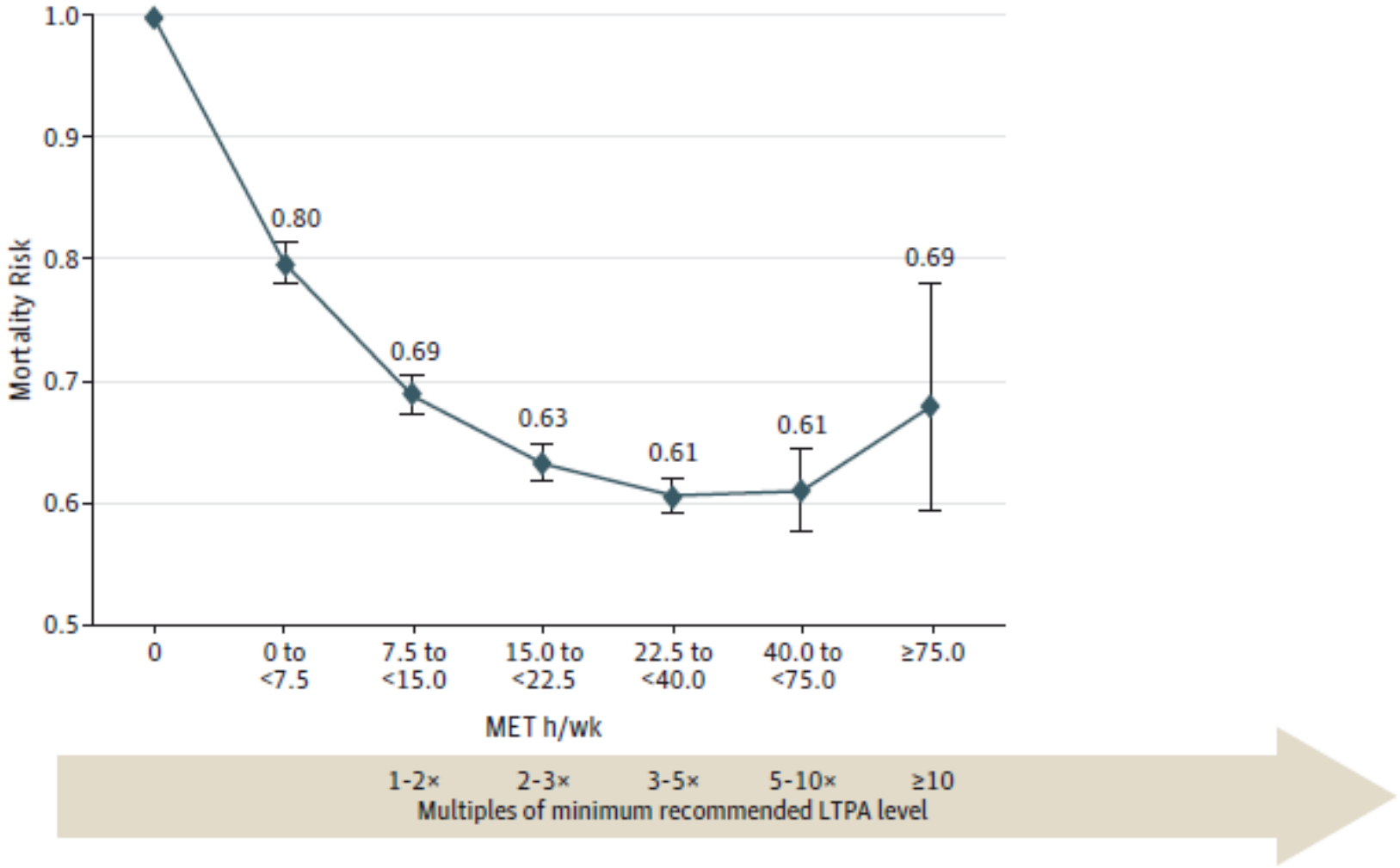
Research

Original Investigation

Leisure Time Physical Activity and Mortality

A Detailed Pooled Analysis of the Dose-Response Relationship

Arem H. et al. JAMA 2015



Arem H. et al. JAMA 2015

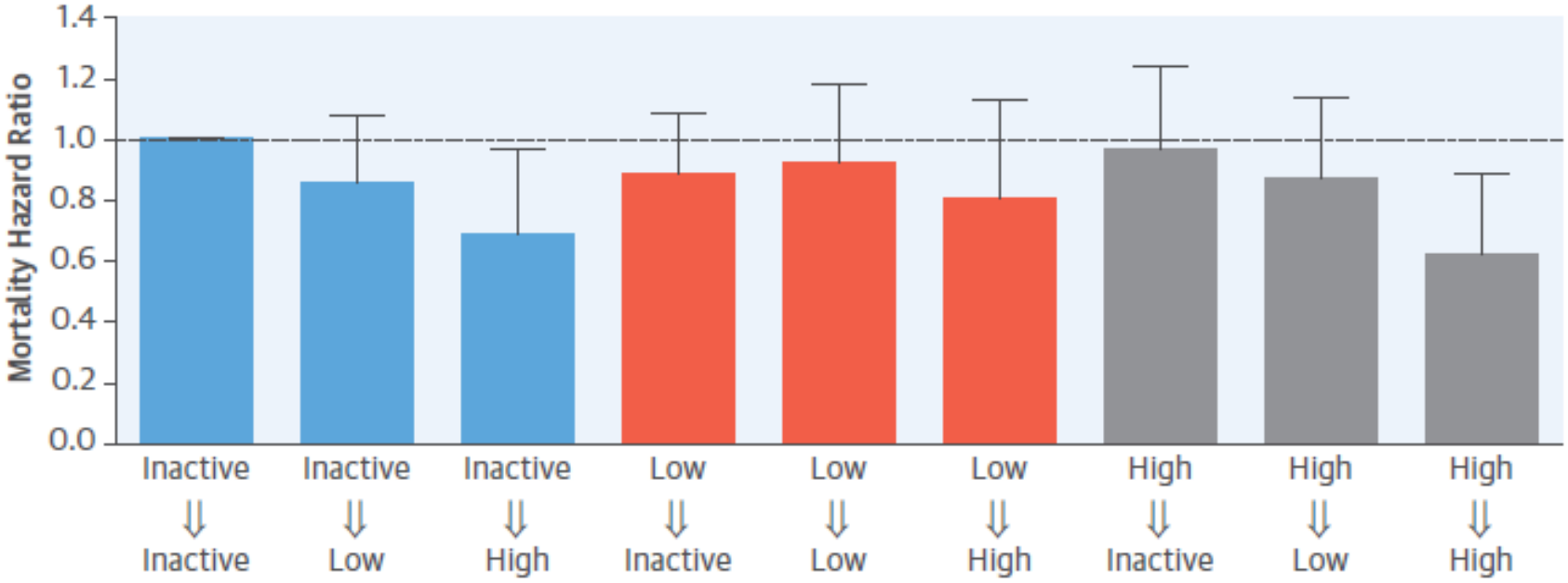
Table 1. Descriptive Characteristics of 661 137 Study Participants

Characteristic	No. of Participants	LTPA Level, MET h/wk, No. (%)[a]						
		0	0.1 to <7.5	7.5 to <15.0	15.0 to <22.5	22.5 to <40.0	40.0 to <75.0	≥75.0
Participants	661 137	52 848 (8.0)	172 203 (26.1)	170 563 (25.8)	118 169 (17.9)	124 446 (18.8)	18 831 (2.9)	4077 (0.6)
Deaths	116 686	11 523 (9.9)	33 511 (28.7)	28 957 (24.8)	19 979 (17.1)	21 114 (18.1)	1390 (1.2)	212 (0.2)
Age, y								
<60	276 418	25 554 (50)	75 671 (45)	71 031 (43)	45 451 (39)	44 721 (36)	11 261 (65)	2729 (76)
60 to <70	307 556	19 694 (39)	75 954 (45)	79 553 (48)	60 978 (53)	66 113 (54)	4631 (27)	633 (18)
≥70	61 356	5924 (12)	16 838 (10)	16 022 (10)	9190 (8)	11 838 (10)	1332 (8)	212 (6)
Sex								
Men	291 485	19 867 (38)	71 564 (42)	74 298 (44)	61 553 (49)	5685 (49)	5685 (30)	1123 (28)
Women	369 652	32 981 (62)	100 639 (58)	96 265 (56)	60 774 (51)	62 893 (51)	13 146 (70)	2954 (72)
Smoking status								
Never	275 388	21 168 (41)	73 112 (43)	72 824 (43)	47 519 (41)	49 729 (41)	8984 (48)	2052 (51)
Former	298 256	21 239 (41)	74 182 (44)	76 979 (46)	56 663 (49)	59 759 (49)	7900 (42)	1534 (38)
Current	74 977	9730 (19)	21 866 (13)	17 721 (11)	11 272 (10)	12 101 (10)	1826 (10)	461 (11)
Alcohol intake								
None	179 676	19 935 (38)	52 463 (30)	44 710 (26)	26 271 (22)	30 912 (25)	4415 (23)	970 (24)
1 Drink/d	376 861	26 750 (51)	95 829 (56)	99 981 (59)	69 817 (59)	69 498 (56)	12 298 (65)	2688 (66)
2 Drinks/d	54 063	2542 (5)	11 550 (7)	13 745 (8)	12 114 (10)	12 609 (10)	1273 (7)	230 (6)
Educational level								
College graduate	250 564	14 324 (29)	61 415 (37)	67 527 (41)	50 433 (44)	48 175 (40)	7257 (44)	1433 (43)
Marital status								
Married	474 338	38 407 (77)	123 151 (77)	123 954 (77)	83 143 (74)	89 568 (76)	13 176 (81)	2939 (76)
BMI								
<25.0	277 193	18 841 (36)	63 975 (38)	70 716 (42)	51 582 (44)	58 629 (48)	11 043 (60)	2407 (60)
25.0 to <30.0	256 713	19 133 (37)	66 709 (39)	67 480 (40)	47 325 (40)	49 015 (40)	5867 (32)	1184 (30)
≥30.0	119 988	14 046 (27)	39 736 (23)	30 758 (18)	18 057 (15)	15 367 (12)	1632 (9)	392 (10)
Race								
White	627 393	49 915 (96)	162 946 (96)	162 468 (97)	111 831 (96)	118 415 (97)	18 042 (96)	3776 (93)
Comorbidities								
Heart disease	61 158	4380 (8)	15 450 (9)	15 462 (9)	12 512 (11)	12 445 (10)	777 (4)	132 (3)
Cancer	46 358	4381 (8)	13 140 (8)	12 214 (7)	7099 (6)	8109 (7)	1198 (6)	217 (5)

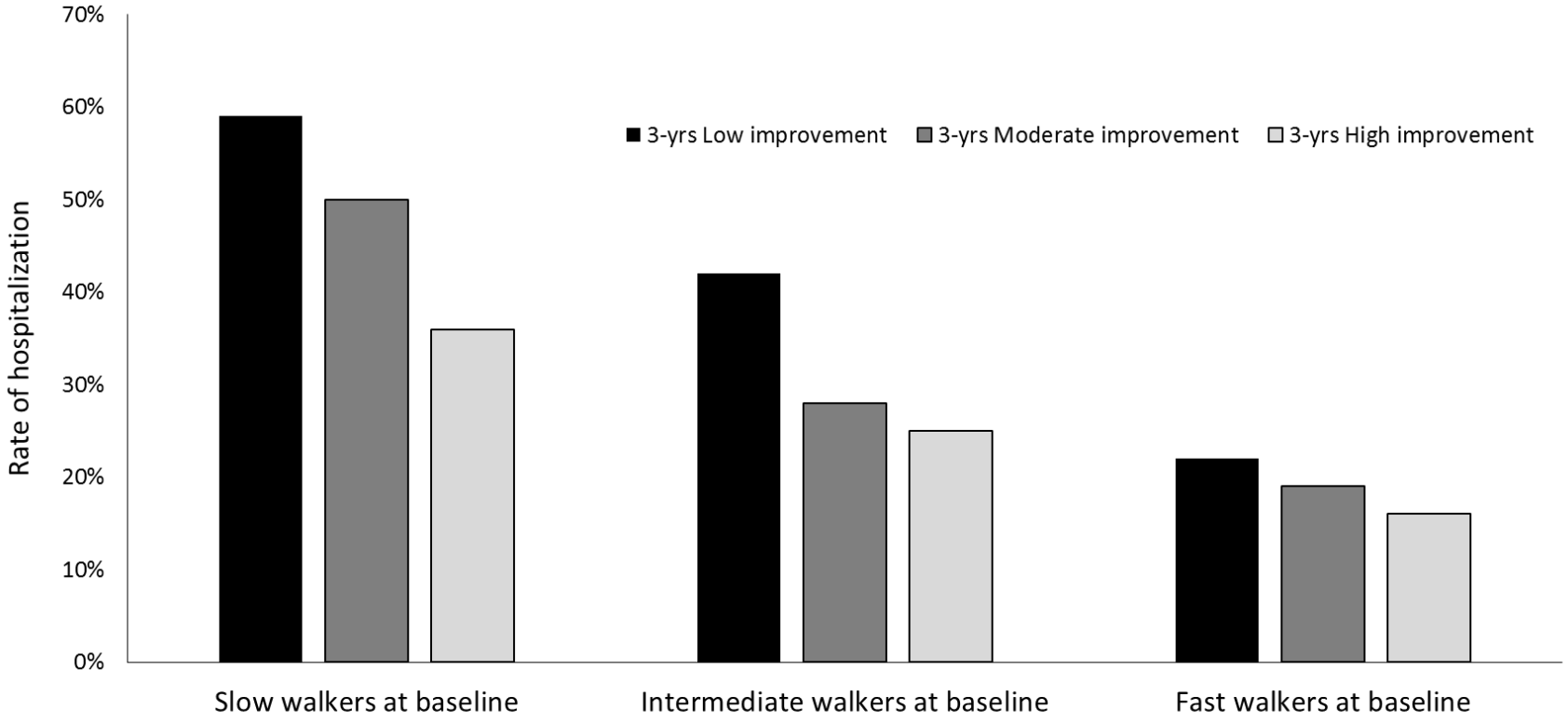
Arem H. et al. JAMA 2015

Sustained Physical Activity, Not Weight Loss, Associated With Improved Survival in Coronary Heart Disease

Moholdt T. et al. JACC 2018



Moholdt T. et al. JACC 2018



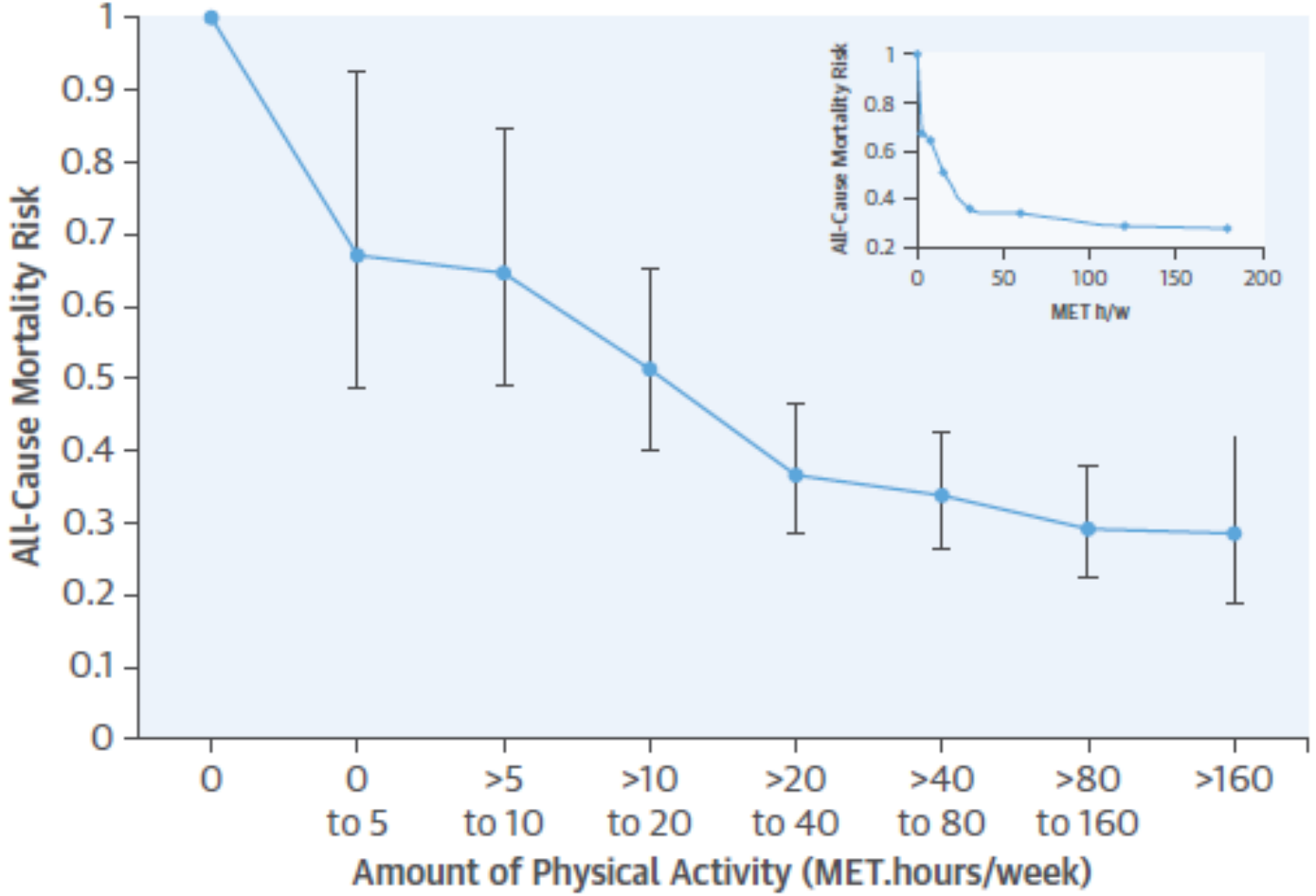
Grazzi G. et al. *Heart* 2016

Physical Activity and Mortality in Patients With Stable Coronary Heart Disease

15,486 patients from 39 countries with stable CHD

Stewart RAH, et al. JACC 2017

All-cause mortality risk associated with each doubling of habitual physical activity volume, and by linear increase in physical activity



Stewart RAH, et al. JACC 2017

Characteristics associated with greatest potential to benefit from increase in physical activity

Sedentary

Limited by dyspnea

↑ ABC-CHD risk score

↑ Age

Smoker

Diabetes

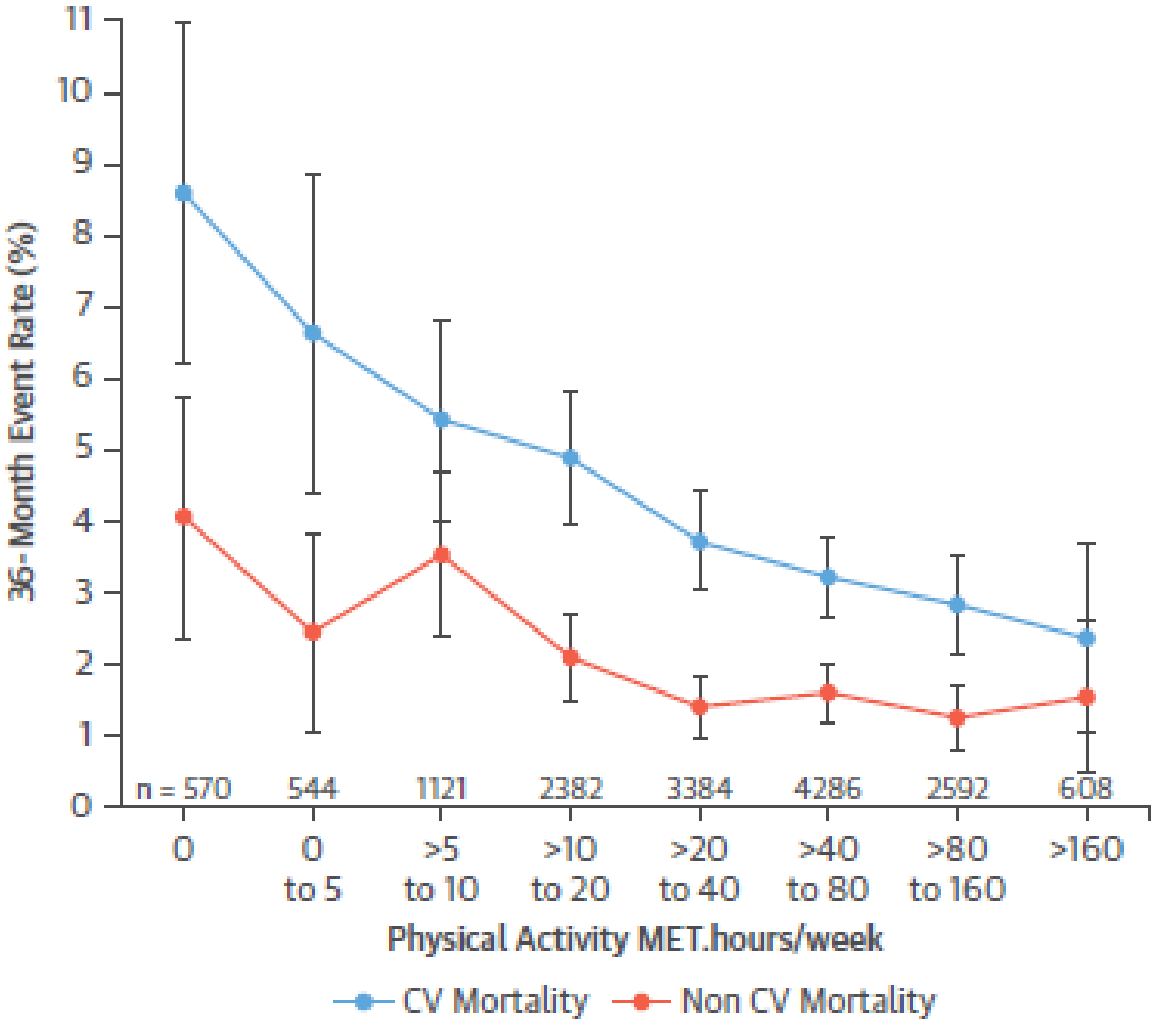
Peripheral artery disease

↑ Troponin T

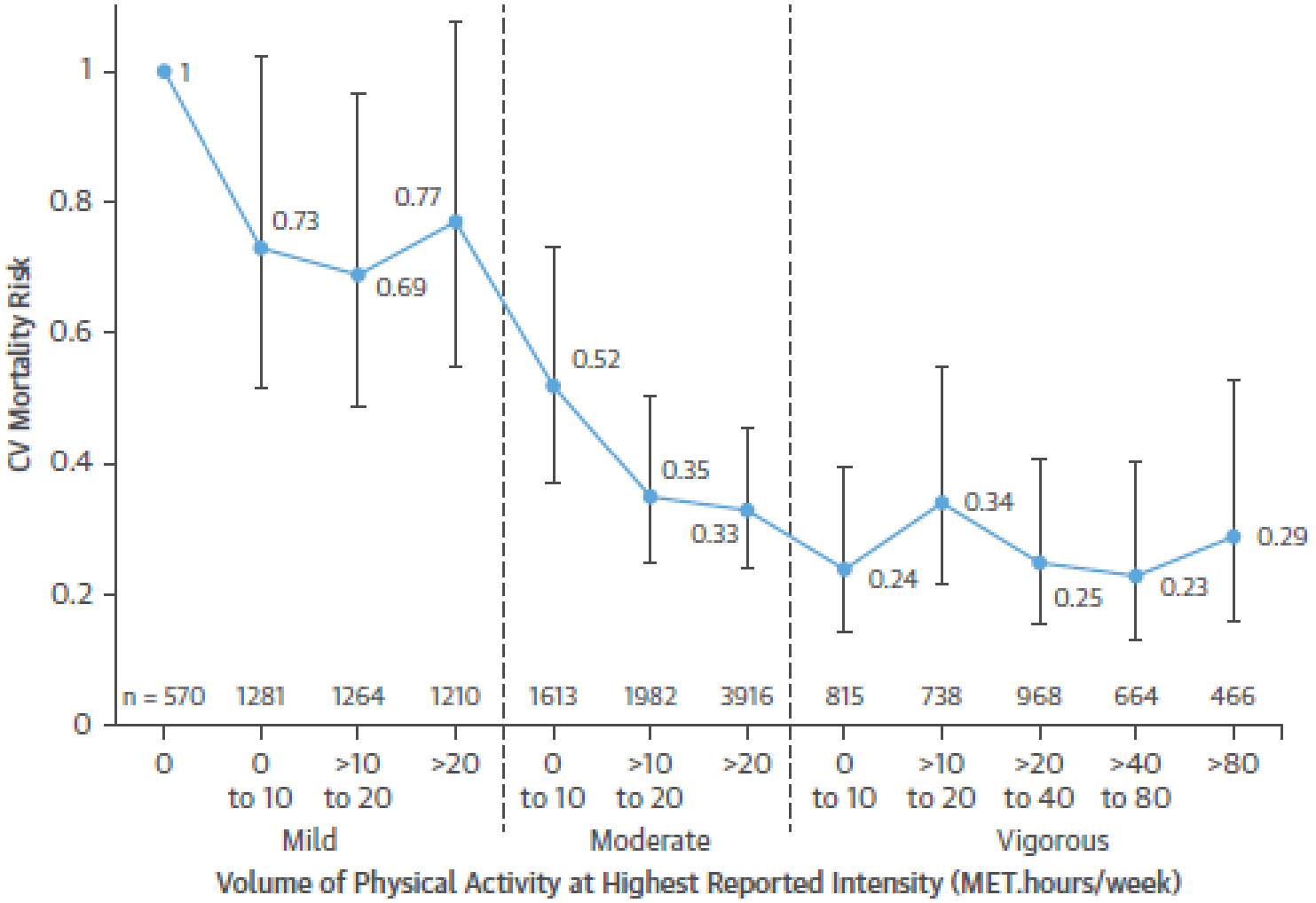
↑ NT-proBNP

↑ LDL cholesterol

Stewart RAH, et al. JACC 2017



Stewart RAH, et al. JACC 2017



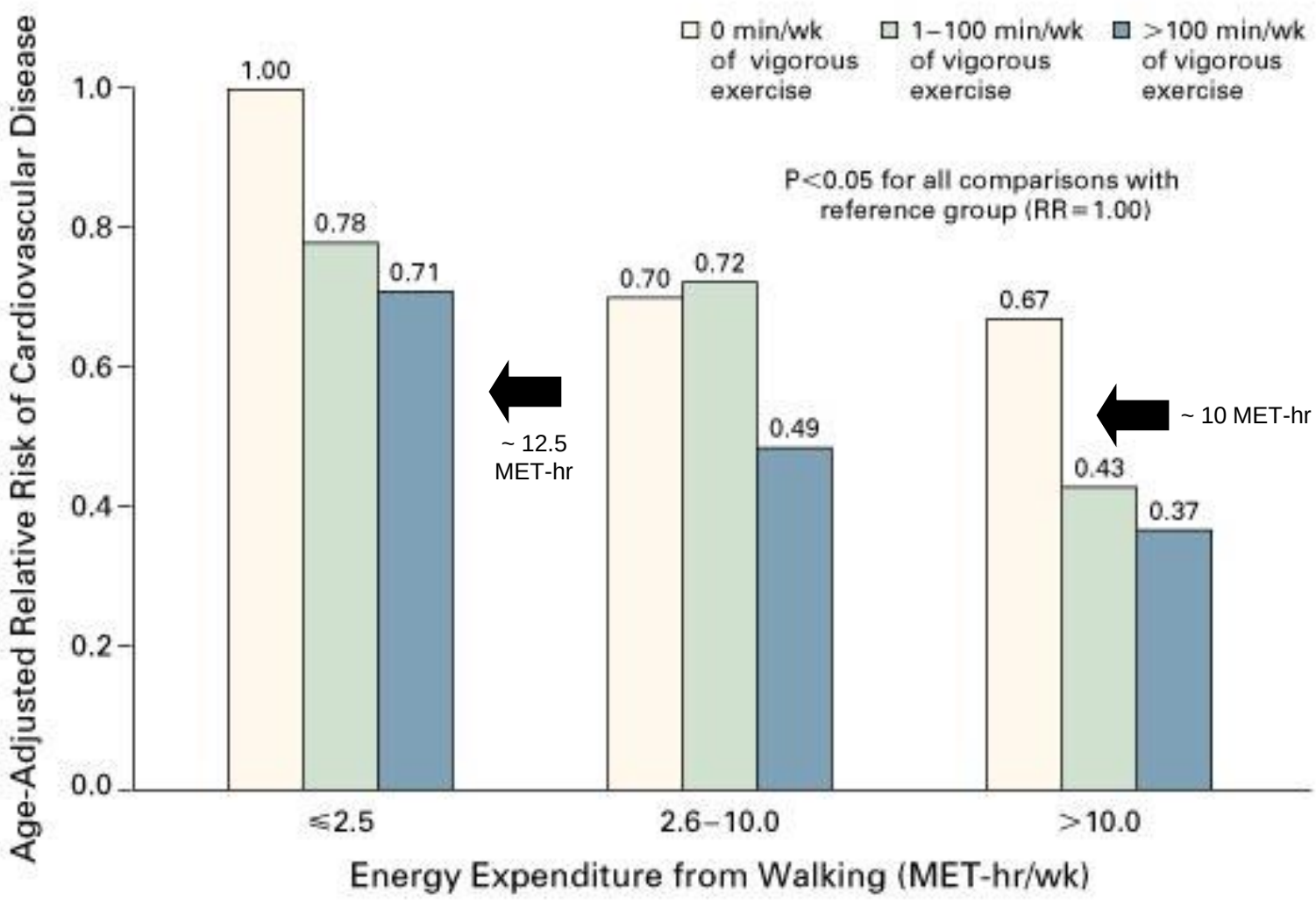
Stewart RAH, et al. JACC 2017

The New England Journal of Medicine

WALKING COMPARED WITH VIGOROUS EXERCISE FOR THE PREVENTION OF CARDIOVASCULAR EVENTS IN WOMEN

73,743 women aged 50 to 79 years

Manson JE. Et al. NEJM 2002



Manson JE. et al. NEJM 2002

frontiers in Public Health

Perceptions of Important Characteristics of Physical Activity Facilities: Implications for Engagement in Walking, Moderate and Vigorous Physical Activity

Heinrich KM, et al. Frontiers in Public Health 2017

- Sebbene il 62% della popolazione adulta negli USA riporti di essere sufficientemente attiva, solo il 10% è risultato effettivamente attivo quando l'attività svolta sia stata oggettivamente misurata e non solo riportata soggettivamente.[1,2]
- L'insufficiente attività fisica rimane dunque un rilevante problema di salute pubblica.

- … Although 62% of US adults report meeting recommendations, only 9.6% of adults do so when objective accelerometer data are used …

Heinrich KM, et al. Frontiers in Public Health 2017

Conclusioni

- Regular exercise is the most effective way to prevent disease.
- Exercise also can help treat many of chronic diseases.
- Moderate exercise is sufficient.
- We know much more about the minimum daily requirement for exercise than about the maximum safe limit.

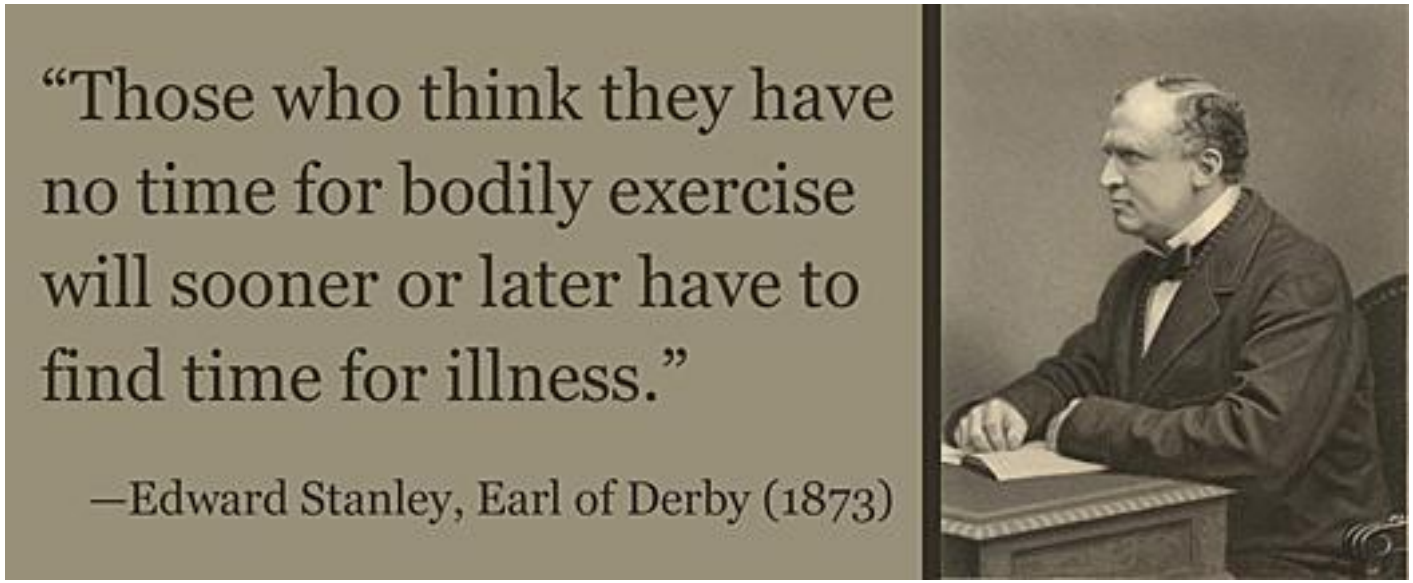
Simon HB. Am J Med 2015

- But we do know that each individual does have a limit, which increases with proper training but decreases with age and when illness or injury intervenes.
- Individuals who choose to push toward their limit should do so with informed consent, knowing that some experts worry they may risk cardiac damage, while others believe intense exercise may attenuate the health benefits of more moderate exercise.
- Walking, jogging, and running will all promote good health, but no one should mistake health as the reason to run a marathon. Still, there are valid personal reasons for high level exercise; if marathon running seems right for you, just be sure to do it right.

Simon HB. Am J Med 2015

- Edward Stanley, the Earl of Derby, got it right in 1873 when he said that those who think they have not time for bodily exercise will sooner or later have to find time for illness.

Simon HB. Am J Med 2015



Edward Stanley, politico, ufficiale, ambasciatore inglese