Cardiac And Metabolic Health Considerations For Return To Running

Mark Cucuzzella MD
Professor of Family Medicine
West Virginia University
Lt Col USAF Reserves Retires

Disclosures

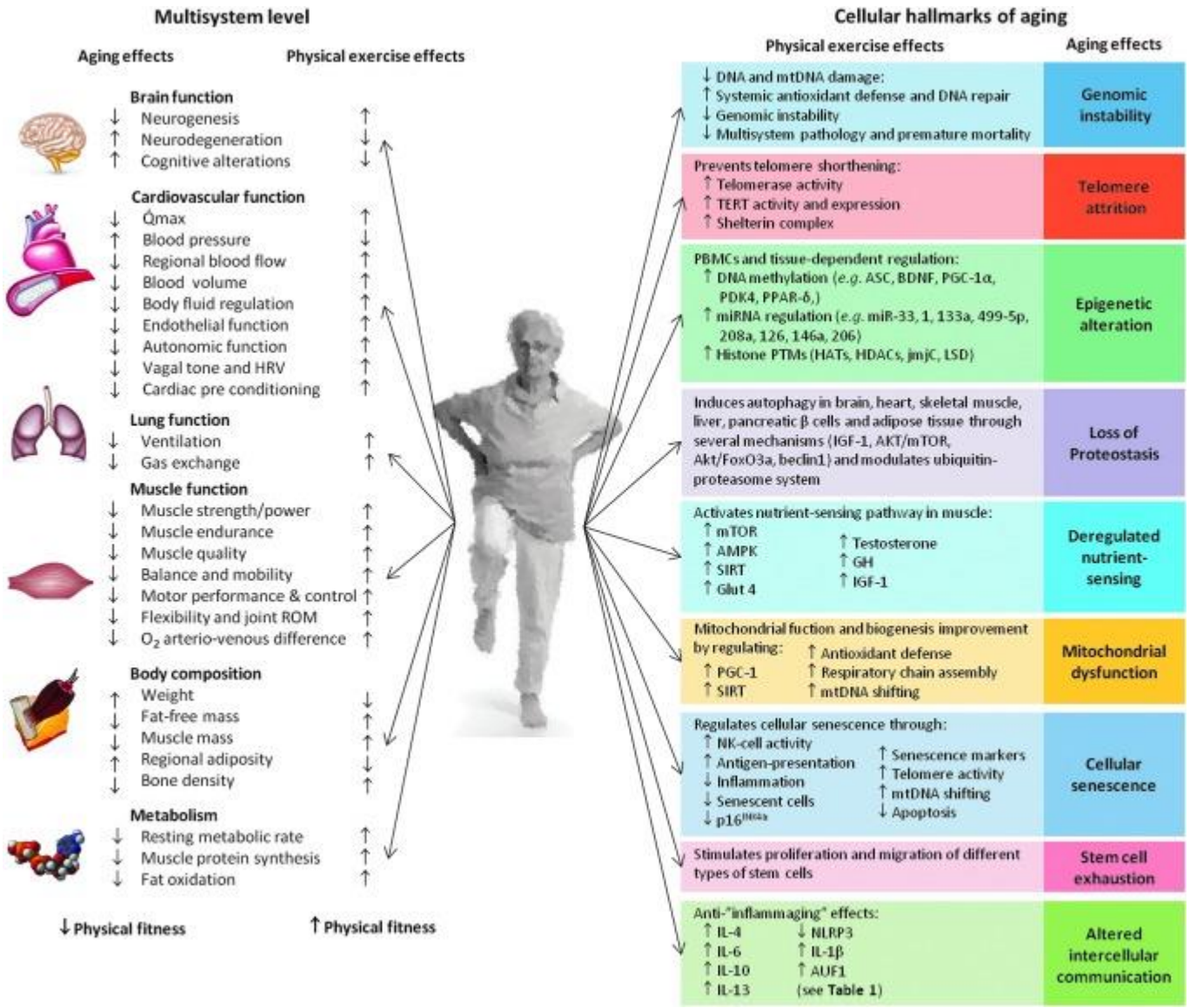
- Own a small shoe store
- Wrote a book- proceeds to non profit
- Board Member Society of Metabolic Health Practitioners
- Founding Member The Nutrition Coalition
- Science Advisory Diet Doctor

Objectives

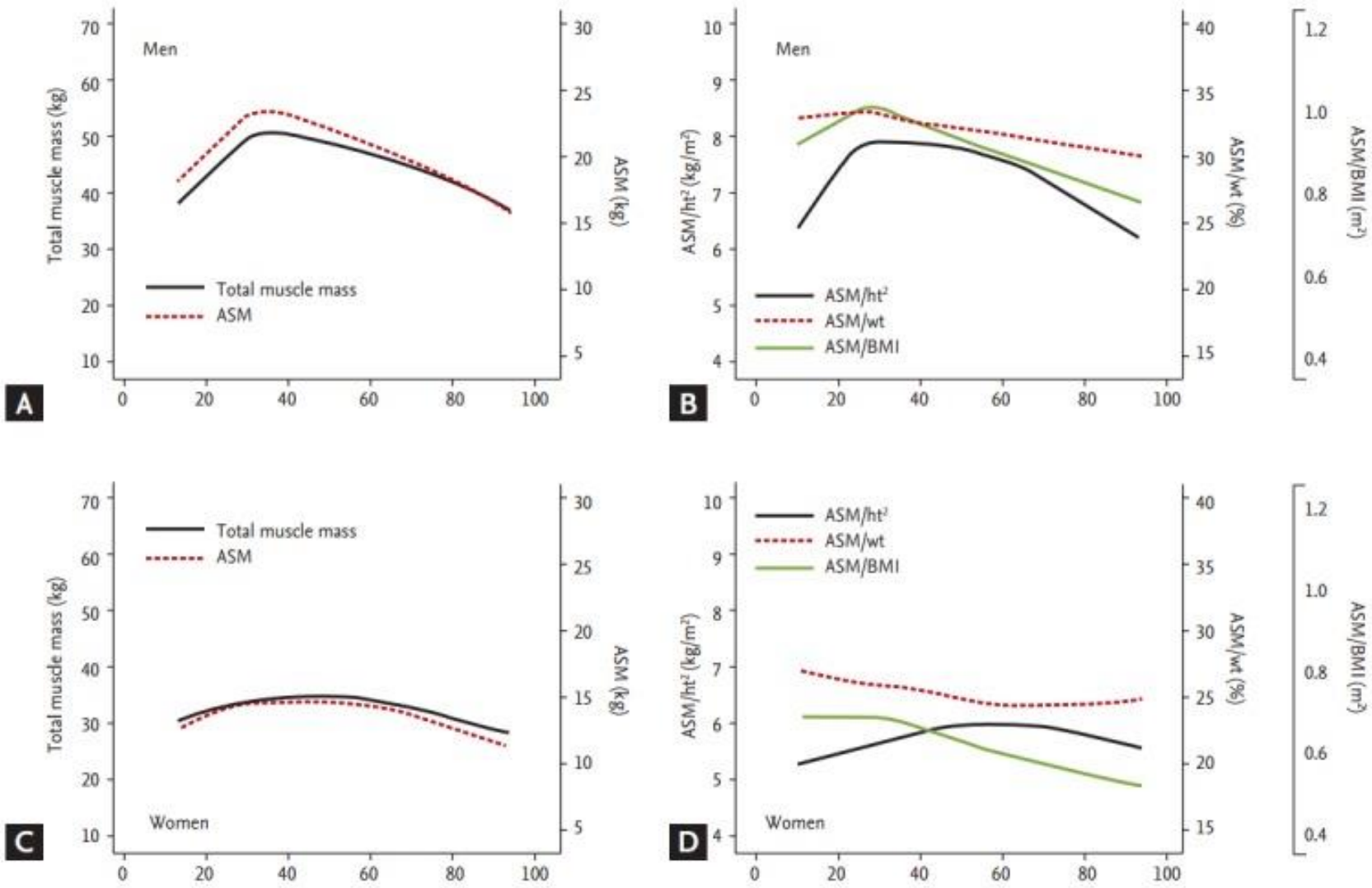
- What is the risk of running?
- Connecting the Mechanisms of Insulin Resistance and CVD
- Metabolic implications?
- Cardiovascular risk assessment

Legend holds the stress of running a distance killed the first marathon runner, Pheidippides, in Athens in 490BC

We are here to give hope
Stress Lab Pt. 92 days- A1c 12.2 to 5.9
35 lb down . Exercising again!



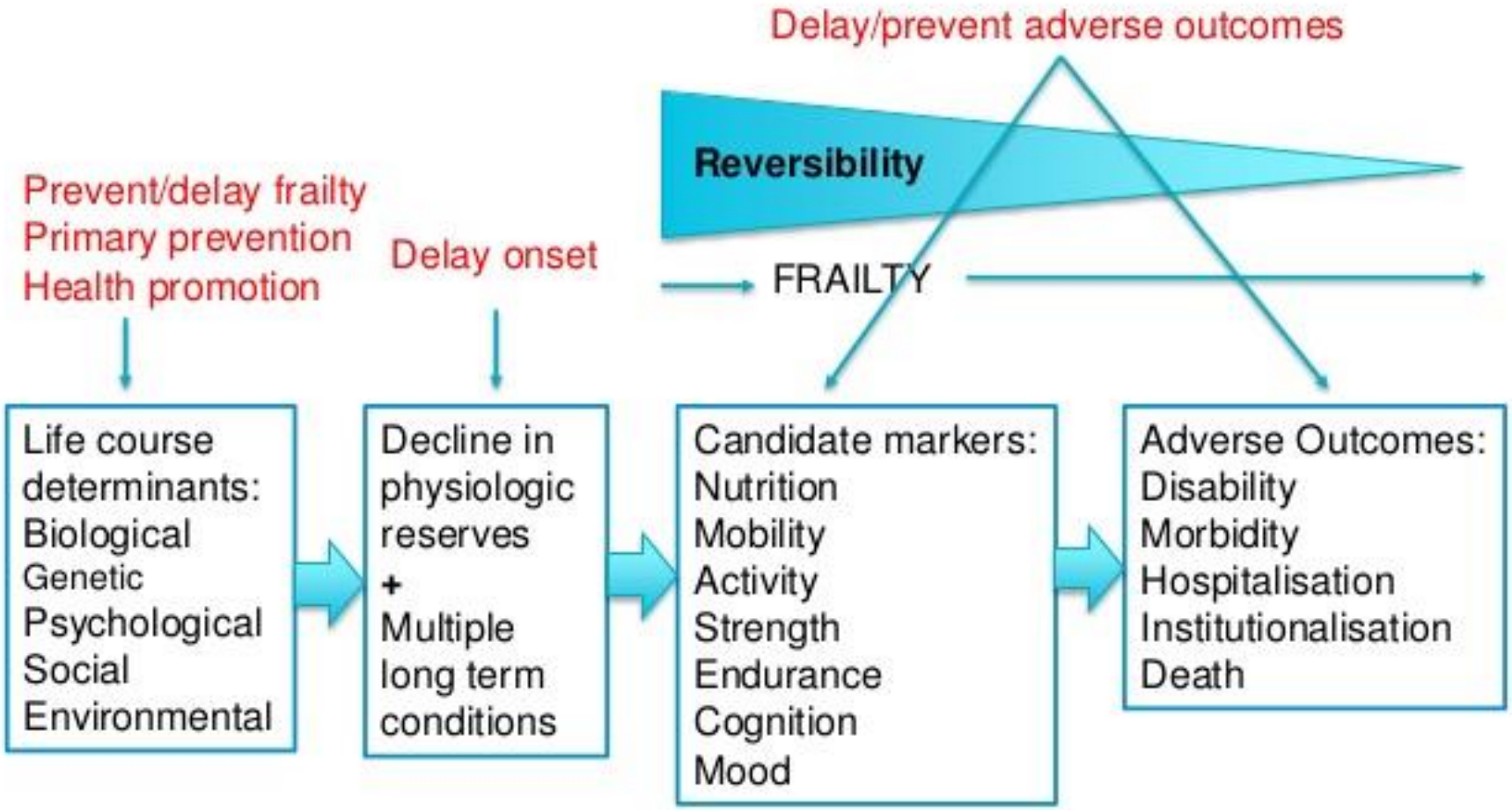
Rejuvenation Res. 2015 Feb 1; 18(1): 57–89. Exercise Attenuates the Major Hallmarks of Aging



doi: 10.3904/kjim.2016.015 Differences among skeletal muscle mass indices derived from height-, weight-, and body mass index-adjusted models in assessing sarcopenia

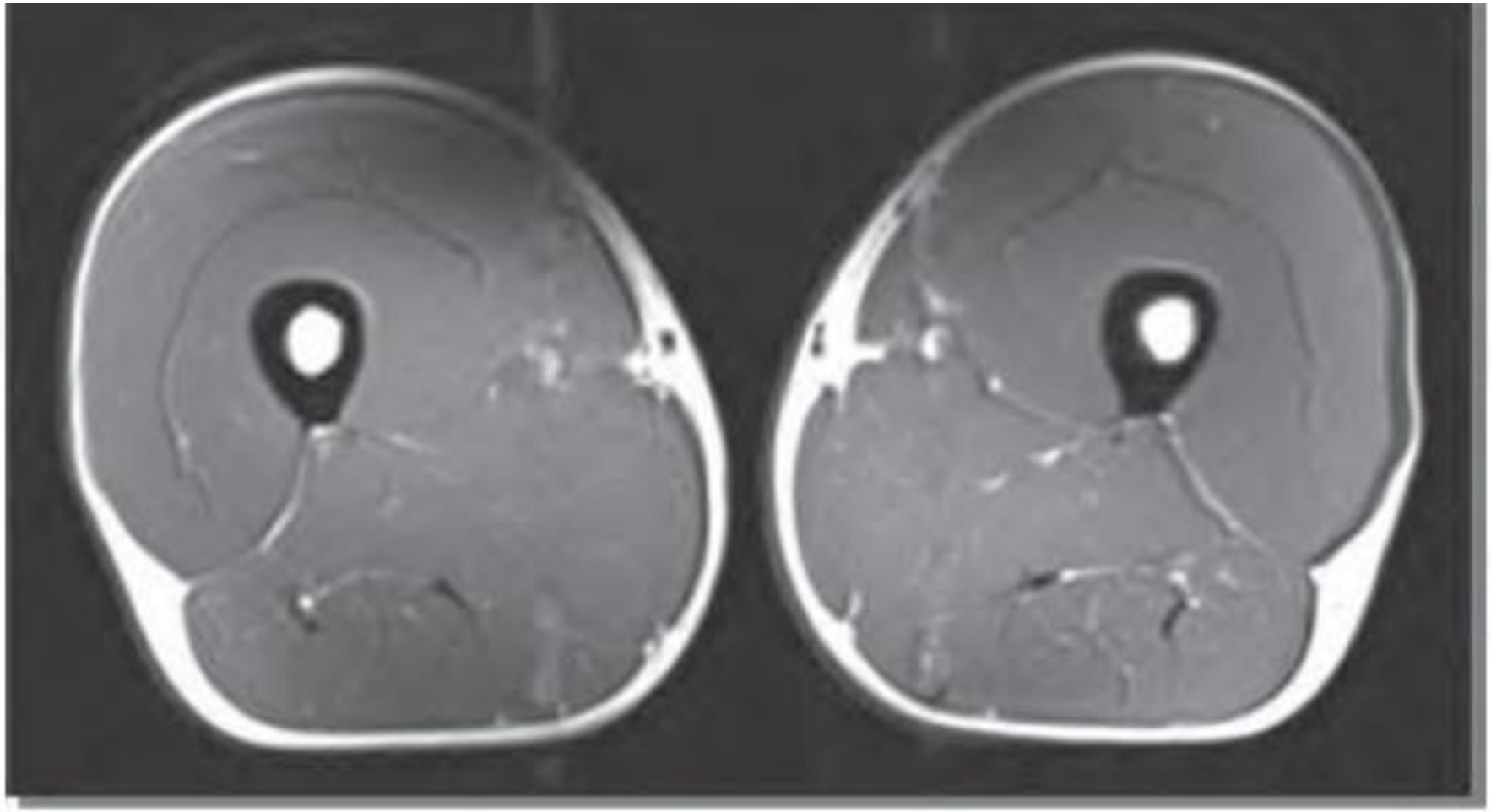
Frailty – a complex syndrome of increased vulnerability

NHS England

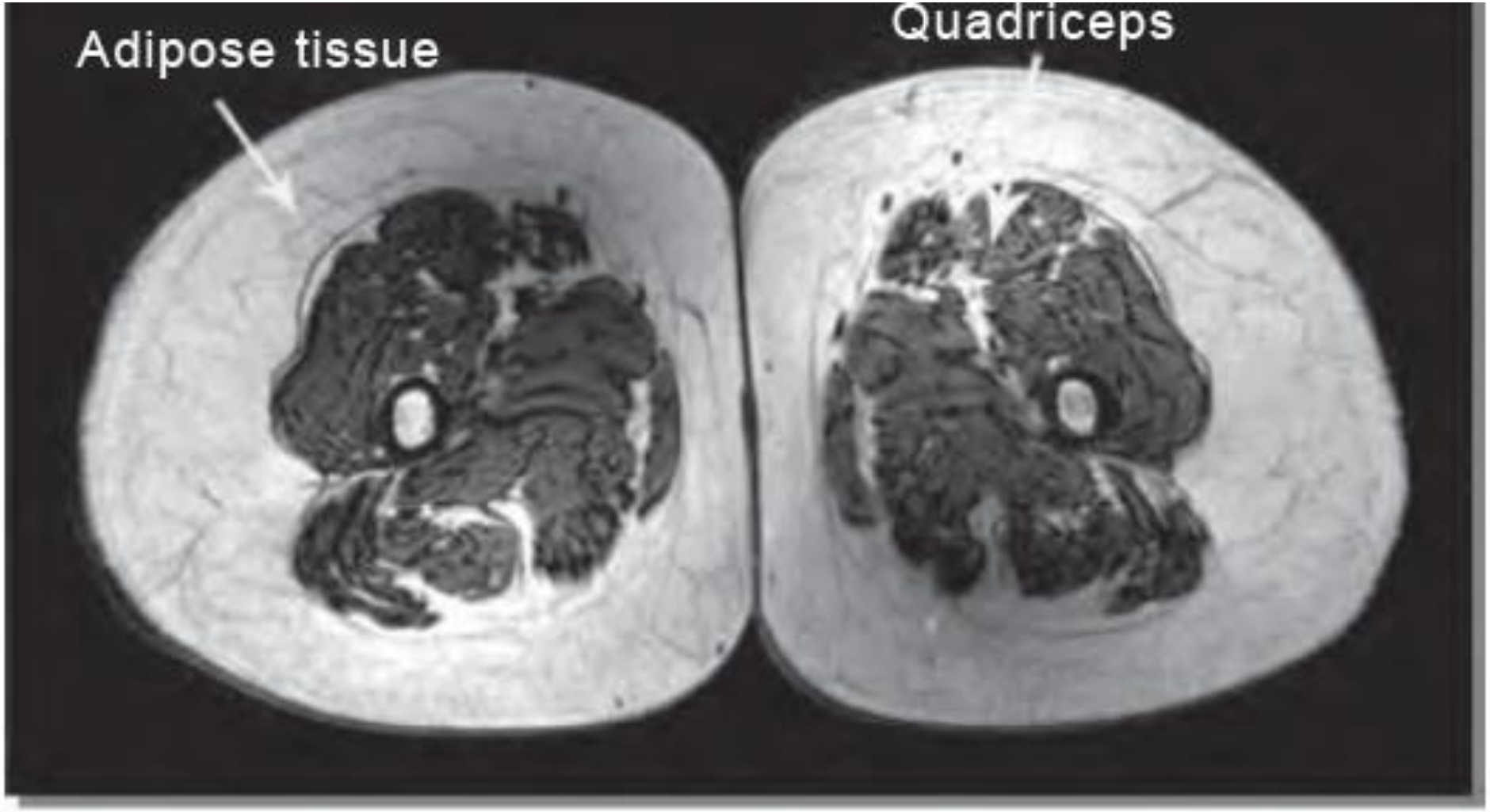


Rodriguez-Mañas L, **Fried** LP. **Frailty** in the clinical scenario. **Lancet**. **2014** Nov 6

Good Muscle Composition



Sarcopenia



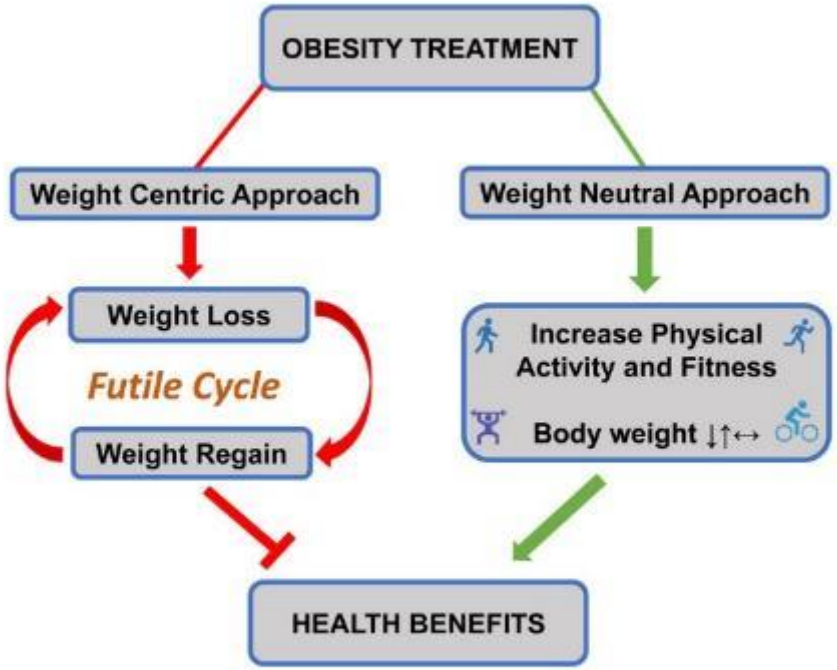
Breaking Down Silos

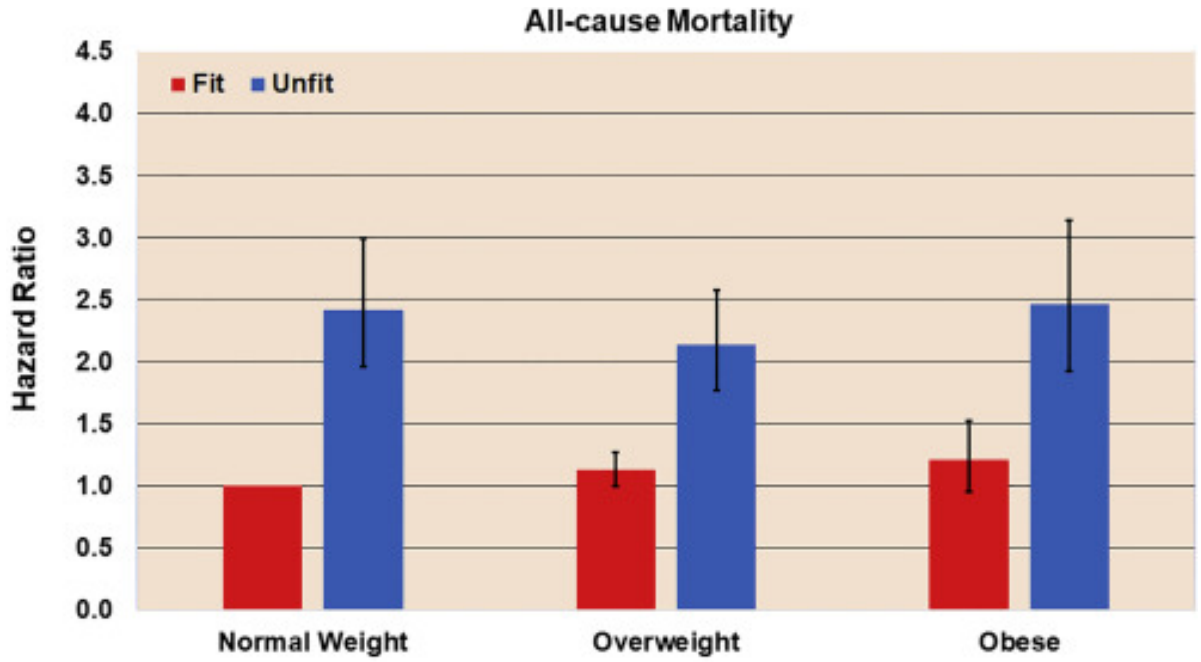
ELSEVIER
Volume 24, Issue 10, 22 October 2021, 102995

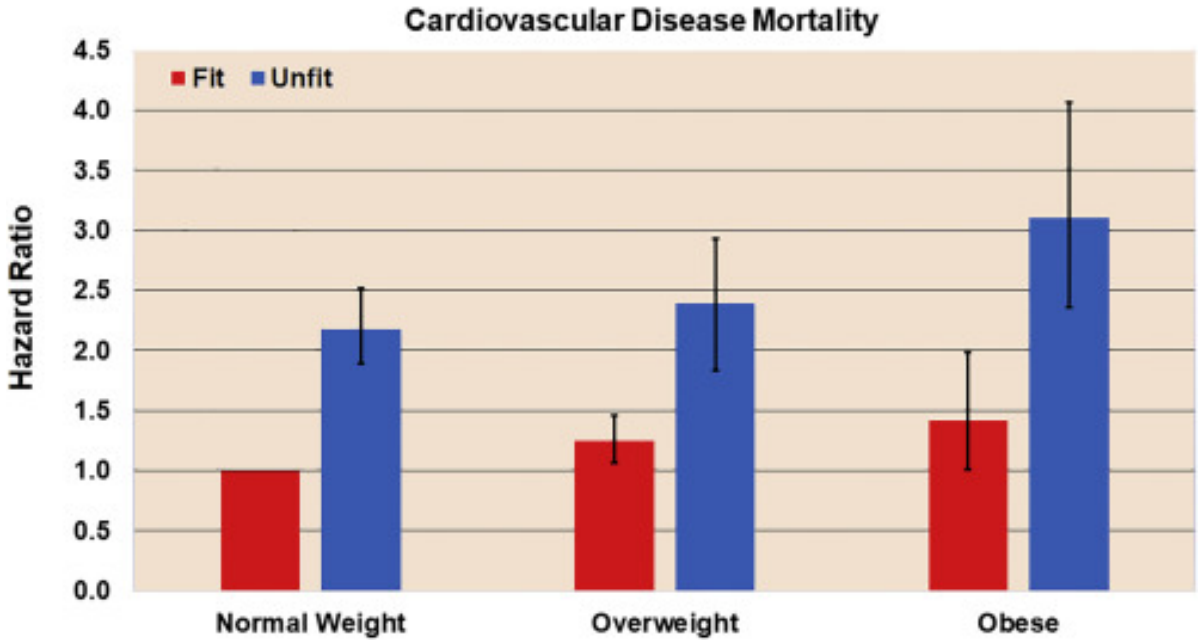
Review

Obesity treatment: Weight loss versus increasing fitness and physical activity for reducing health risks

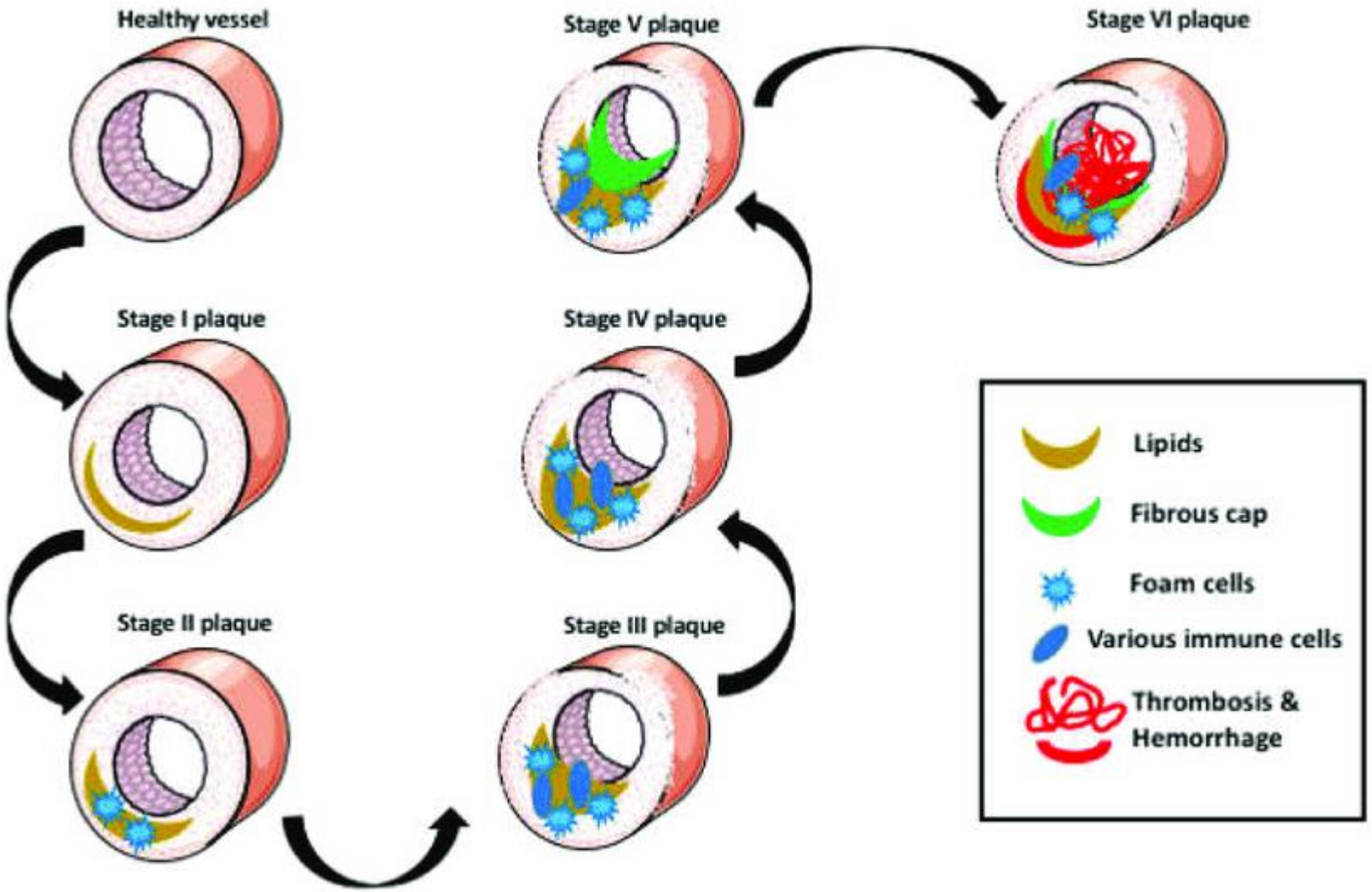
Glenn A. Gaesser [1], Siddhartha S. Angadi [2]



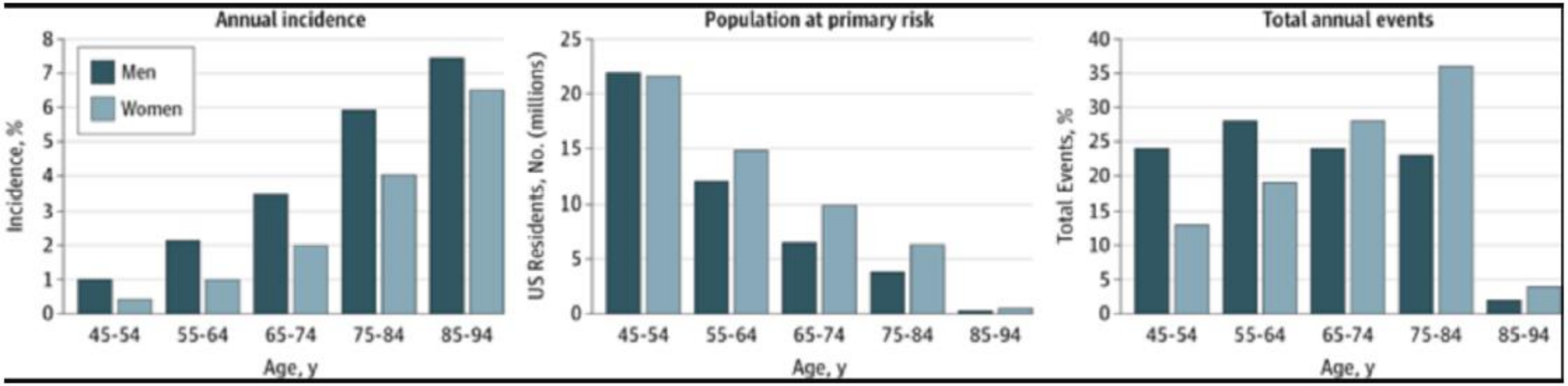

All-cause Mortality
Fit
Unfit
Hazard Ratio
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Normal Weight
Overweight
Obese


Cardiovascular Disease Mortality
Fit
Unfit
Hazard Ratio
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Normal Weight
Overweight
Obese

CVD Process Takes Decades

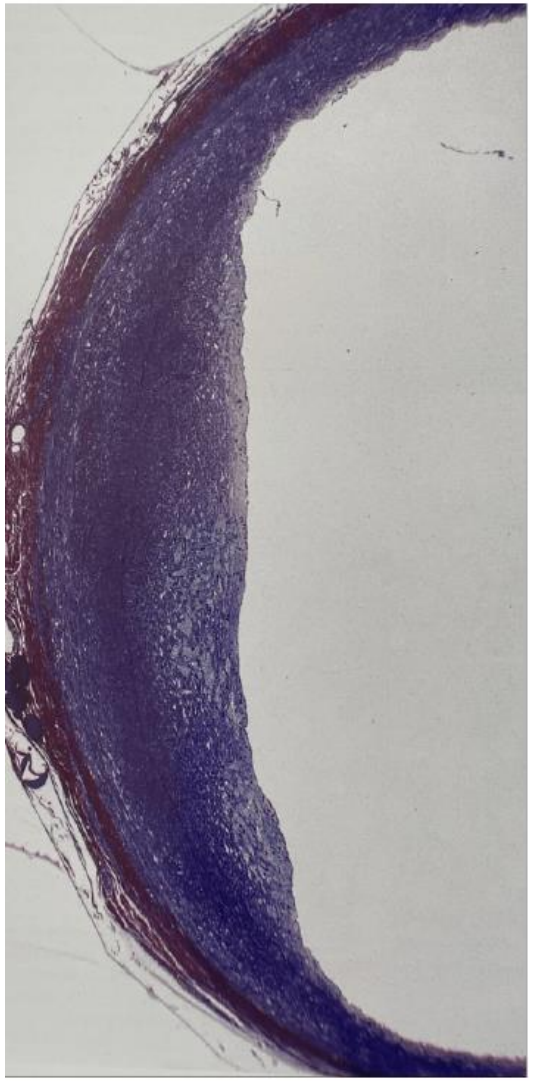


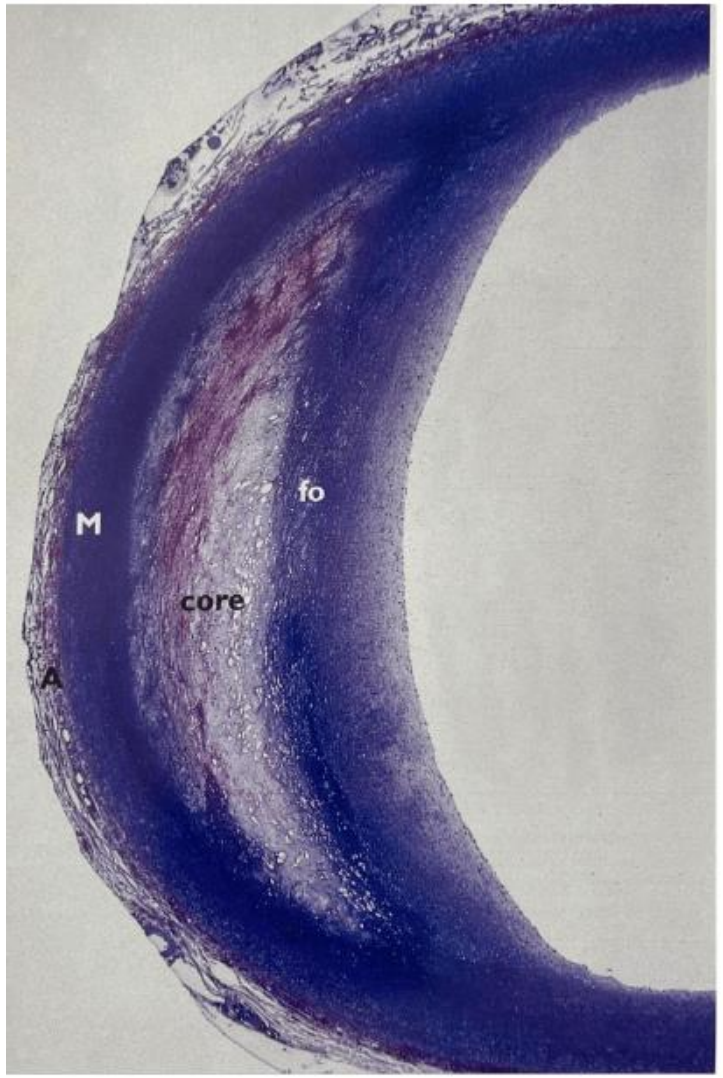
Not just a disease of the aged



Sniderman AD, Thanassoulis G, Williams K, Pencina M. Risk of Premature Cardiovascular Disease vs the Number of Premature Cardiovascular Events. *JAMA Cardiol.* 2016;1(4):492–494. doi:10.1001/jamacardio.2016.0991

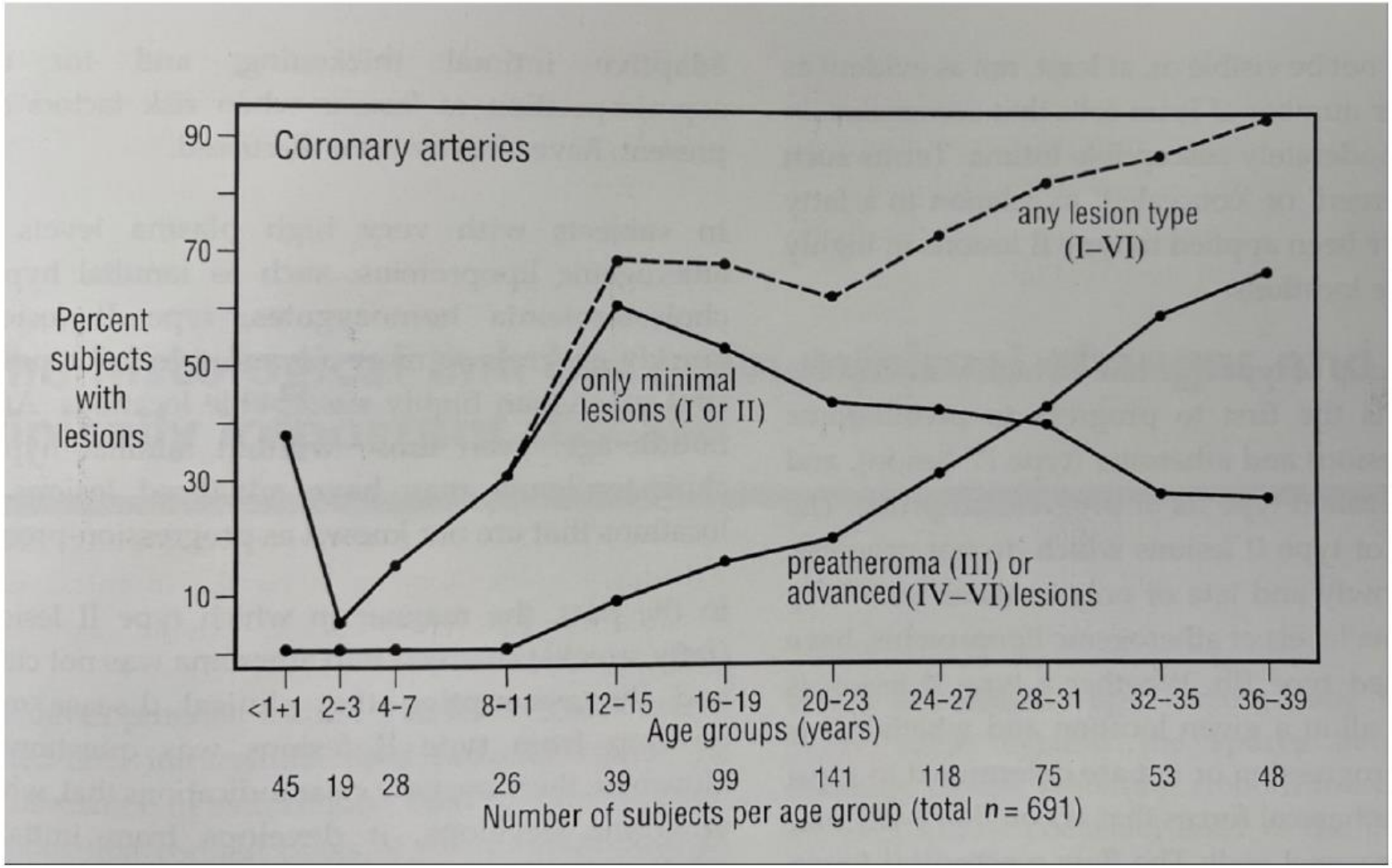
What Can We Learn From Autopsies? Young accident victims. Type II, IV, V lesions- no calcification yet !





Atlas of Atherosclerosis Progression and Regression (Encyclopedia of Visual Medicine Series) 2nd Edition
by Herbert C. Stary (Author)

What Can We Learn From Autopsies?



Atlas of Atherosclerosis Progression and Regression (Encyclopedia of Visual Medicine Series) 2nd Edition by Herbert C. Stary (Author)

What is this based on????

From runner's face to dodgy knees: Why running helps keep women young, but ages men

As a new study shows running can age men's vascular health by a decade, is running really a friend or foe as we get older?

Endurance events such as marathons and triathlons were found to boost women's health, reducing their vascular age by an average of six years (Photo: Westend61/Getty)

Men, be warned. Running marathons could actually age you

Males over 40 could be putting themselves at greater risk of heart attacks and strokes by taking part in the gruelling events, say experts

By Laura Donnelly, HEALTH EDITOR
7 June 2022 • 6:00am

Men who regularly took part in endurance events were found to have a vascular age a decade older than their chronological age | CREDIT: Jeff Gilbert for The Telegraph

Imaging

145 Masters athletes demonstrate sex differences in aortic stiffness

PDF

FREE

Rebecca Hughes [1], Natalia Ojrzynska-Witek [2], Joao Augusto [2], Anish Bhuva [2], Gemma Parry-Williams [3], Stathis Papatheodorou [3], Andrew D'Silva [2], Camilla Torlasco [4], Charlotte Manisty [2], Alun Hughes [5], Sanjay Sharma [3], James Moon [2]

- Published abstract- No Refs No Peer Review
- 150 men and 150 women, all of whom were athletes over the age of 40 – mostly runners
- Compared to non-athletes, the men had significantly stiffer aortas, while the women didn't
- wouldn't have made waves if they hadn't translated the stiffness findings into a "vascular age"

Extreme Activity Good??

triathlete

KONA HUB GEAR TRAINING NUTRITION CULTURE EVENTS

TRAVEL NEWS PEOPLE

Tim O'Donnell Reveals He Suffered Heart Attack During Challenge Miami

The type of heart attack is colloquially known as "the widowmaker"—but the Kona runner-up says he's doing better now.

AUGUST 12, 2021
SUSAN LACKE

Anker gives a thumbs-up while in the hospital in Kathmandu, Nepal. Anker arrived at the hospital nine hours after his heart attack at nearly 20,000 feet.
PHOTOGRAPH COURTESY CONRAD ANKER

ADVENTURE | NEWS

Exclusive: Celebrated Mountaineer Suffers Heart Attack at 20,000 Feet

My go to guy: The Man with 8 Tweets **Dr Andre La Gerche**
https://twitter.com/ALaGerche

His first 4 tweets related to this story Sept 2017

Bundall Today 13 °/ 21 °

Gold Coast Bulletin

My News Local Queensland National World Opinion Business Entertainment Lifestyle Sport

Lifestyle

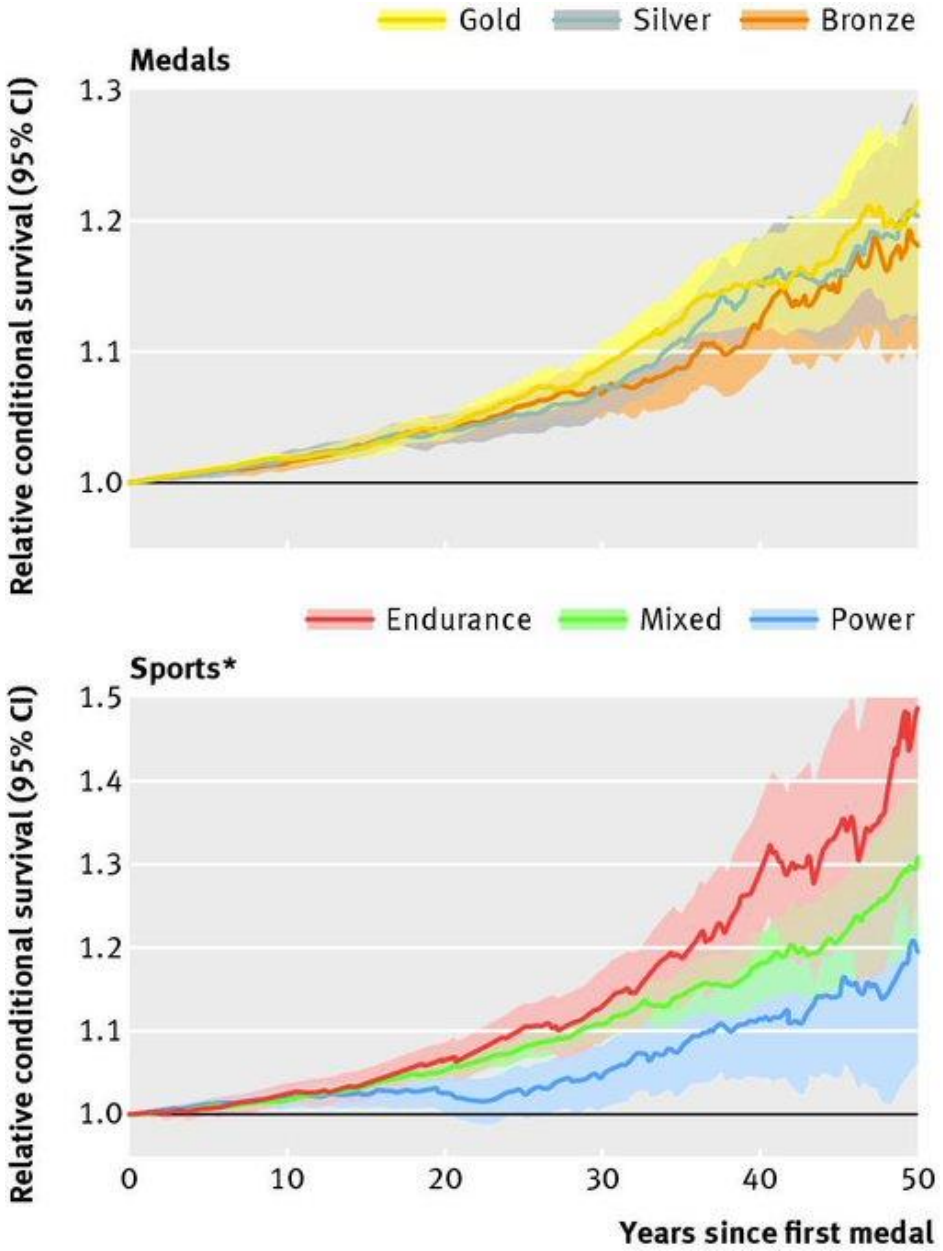
Why did fit former ironman Dean Mercer's heart fail?

HE was a super fit bloke and the least likely person to suffer a heart attack. Or so we thought. A cardiologist explains why former ironman Dean Mercer's heart gave out. And issues a warning for athletes over 40.

Dwayne Grant

First 4 tweets Sept 2017

- "Irresponsible and ill-informed.“
- "Cardiologists should know there is no proven link between endurance sport and sudden death. Research suggests opposite."
- "Athletes live longer. Endurance athletes and gold medallists live the longest. Have faith fellow athletes."
- "Too sad that people are using a tragic event to push unproven agendas. Great man, sad event, no blame!"



My friend and co Race and Camp Director Katie Thompson
Rim To River 100 Mile after cardiac event
Dr La Gerche weighed in ☺

From: **Association of Cardiorespiratory Fitness With Long-term Mortality Among Adults Undergoing Exercise Treadmill Testing**

JAMA Netw Open. 2018;1(6):e183605. doi:10.1001/jamanetworkopen.2018.3605

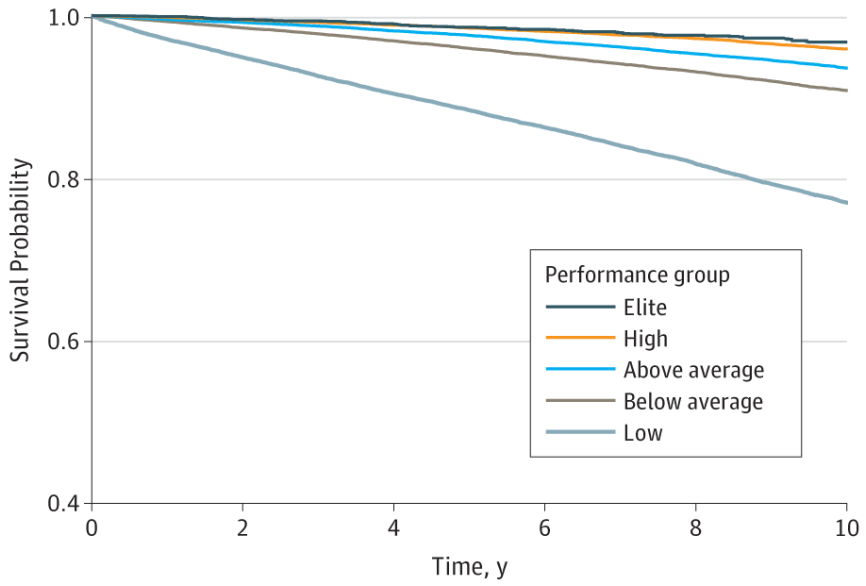
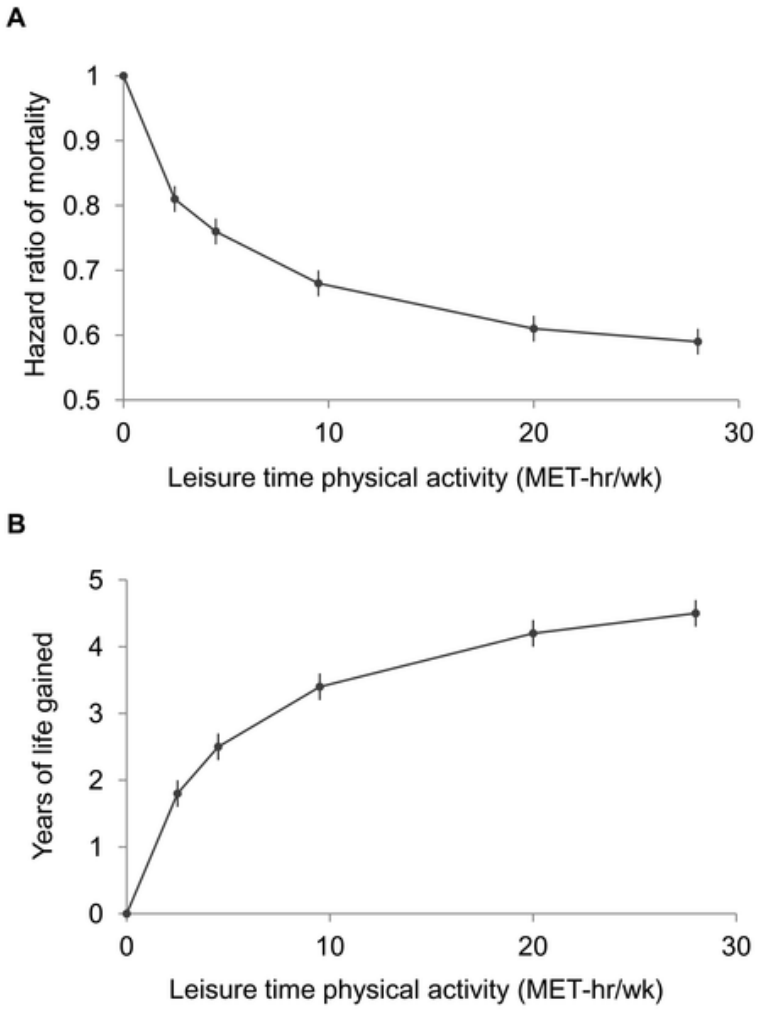


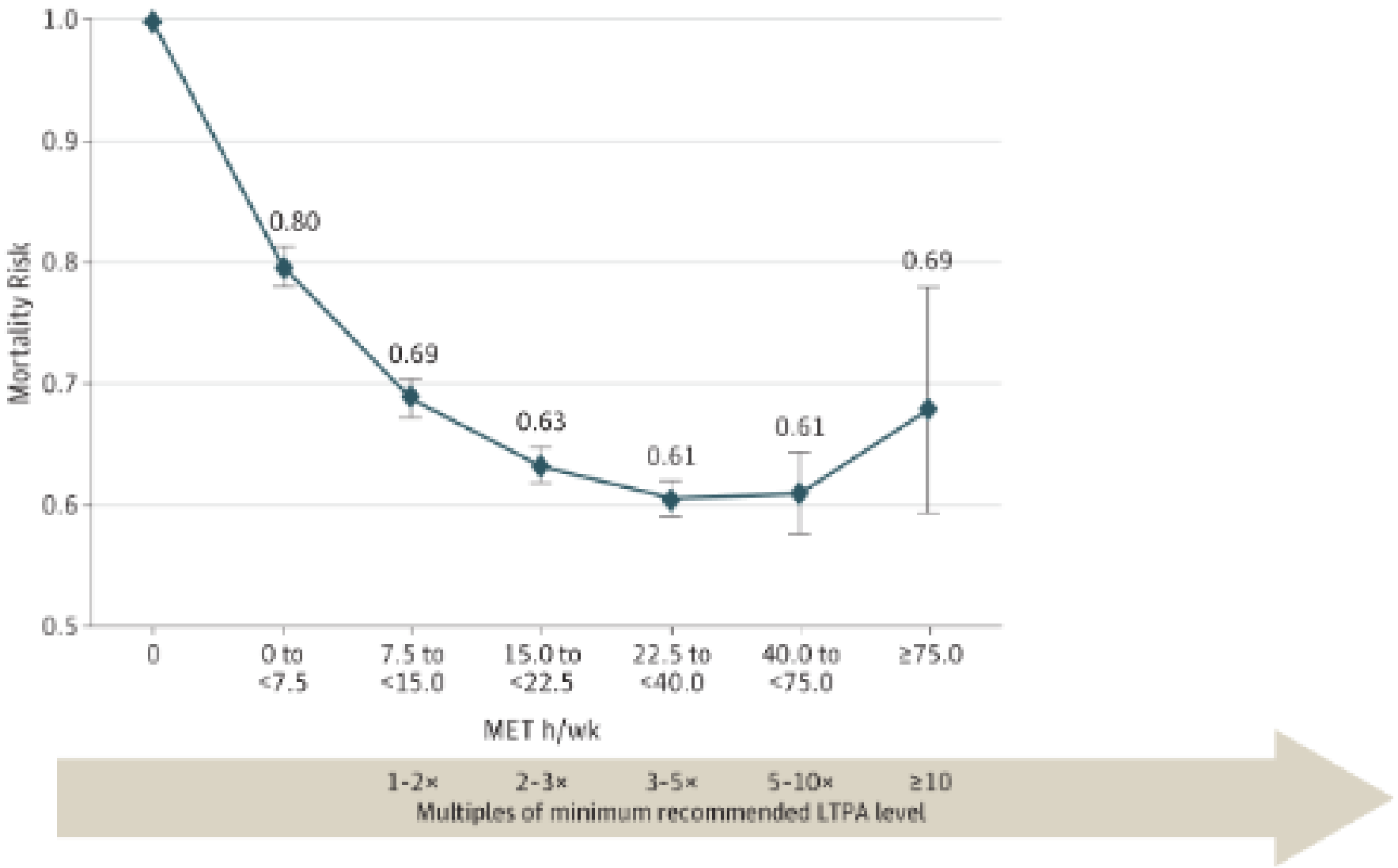
Figure Legend:

Patient Survival by Performance GroupLog-rank P < .001 for all groups, except elite vs high performers (log-rank P = .002). Performance group classifications by cardiorespiratory fitness are defined in Table 2.

Figure 1. Leisure time physical activity level and hazard ratios for mortality and gains in life expectancy after age 40.



Moore SC, Patel AV, Matthews CE, Berrington de Gonzalez A, Park Y, et al. (2012) Leisure Time Physical Activity of Moderate to Vigorous Intensity and Mortality: A Large Pooled Cohort Analysis. PLOS Medicine 9(11): e1001335. https://doi.org/10.1371/journal.pmed.1001335
https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001335



JAMA Intern Med. 2015;175(6):959-967
Leisure Time Physical Activity and Mortality A Detailed Pooled Analysis of the Dose-Response Relationship

Invest in Mets- Not in Meds

MET score	Description
1.0 - 1.5	Sedentary
1.6 - 2.9	Light intensity
3.0 - 5.9	Moderate intensity
6.0 +	Vigorous intensity

Leisure activities	METs	Sports activities	METs
Watching TV	1.0	Golf	4.8
Sitting, writing, reading, desk work	1.3	Boxing, punching bags	5.5
Cleaning, sweeping carpets	3.3	Rock climbing	5.8
Walking the dog	3.0	Resistance training, vigorous effort	6.0
Bicycling, leisure < 10 mph	4.0	Basketball, non-competitive	6.5
Gardening, moderate effort	4.3	Bicycling, stationary 90-100 watts	6.8
Mowing lawn	5.5	Rowing, stationary, 100 watts	7.0
Moving furniture, carrying boxes	5.8	Jogging	7.0
Backpacking, hiking	7.8	Soccer, non-competitive	7.0
		Dancing, aerobic general	7.3
		Calisthenics, vigorous effort push ups, sit ups, pull ups, jumping	8.0
		Running, 6 mph (10 min/mile)	9.8
		Rope jumping, 100-120 skips/min	11.8
		Running, 10 mph (6 min/mile)	14.5

Dr Paul Williams “Runners Study”

> Atherosclerosis. 2010 Apr;209(2):524-7. doi: 10.1016/j.atherosclerosis.2009.09.018.
Epub 2009 Sep 16.

Reductions in incident coronary heart disease risk above guideline physical activity levels in men

Paul T Williams [1]

Affiliations + expand

PMID: 19815208 PMCID: PMC3776591 DOI: 10.1016/j.atherosclerosis.2009.09.018

Free PMC article

- Conclusions: ***Exceeding guideline physical activity levels produce important CHD-risk reductions***.

This Issue

Article

January 27, 1997

Relationship of Distance Run per Week to Coronary Heart Disease Risk Factors in 8283 Male Runners

The National Runners' Health Study

Paul T. Williams, PhD

» Author Affiliations

Arch Intern Med. 1997;157(2):191-198. doi:10.1001/archinte.1997.00440230063008

- Conclusions: Our data (1) suggest that substantial health benefits occur at exercise levels that exceed current minimum guidelines and (2**) do not exhibit a point of diminishing return to the health benefits of running at any distance less than 80 km/wk**

Review

Association of high amounts of physical activity with mortality risk: a systematic review and meta-analysis FREE

Kim Blond [1, 2, 3], Cecilie Fau Brinkløv [1], Mathias Ried-Larsen [1], Alessio Crippa [4], Anders Grøntved [3]

Correspondence to Kim Blond, Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark; kim.blond.01@regionh.dk

BJSM 2018

Compared with the recommended level, mortality risk was lower at physical activity levels well above the recommended target range. Further, there was **no threshold beyond which lifespan was compromised**.

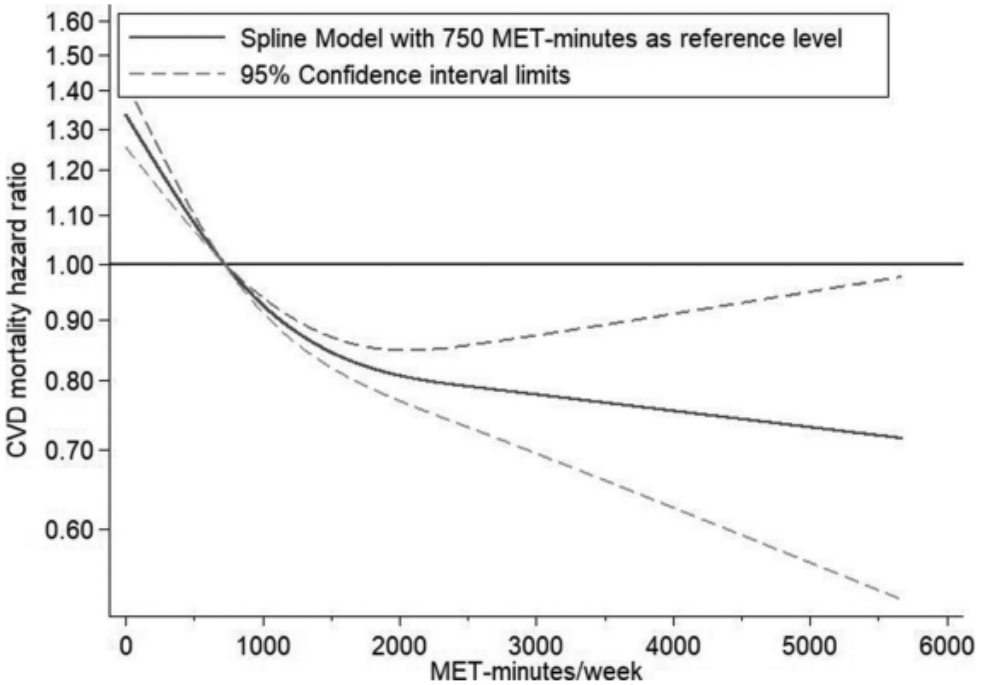
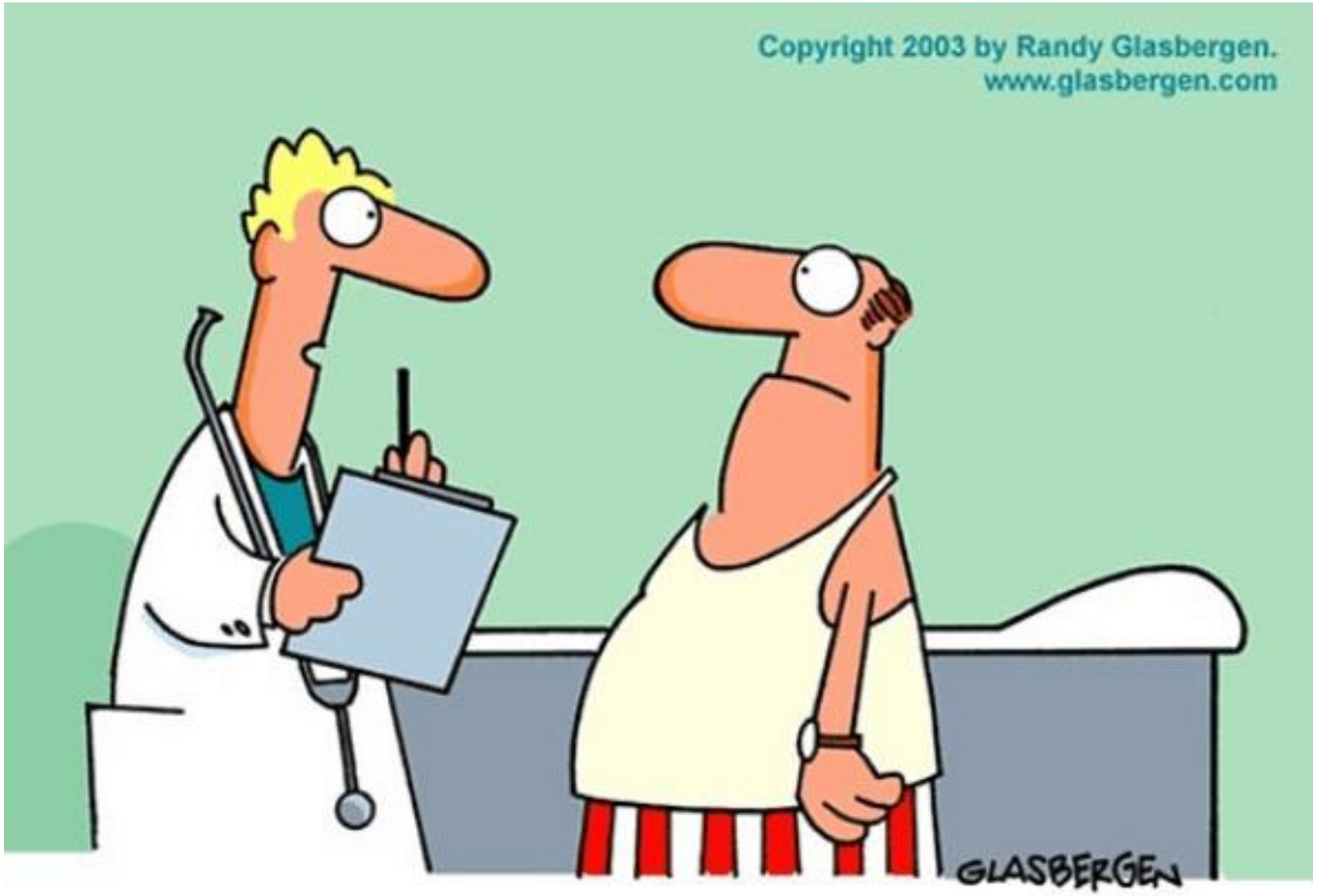
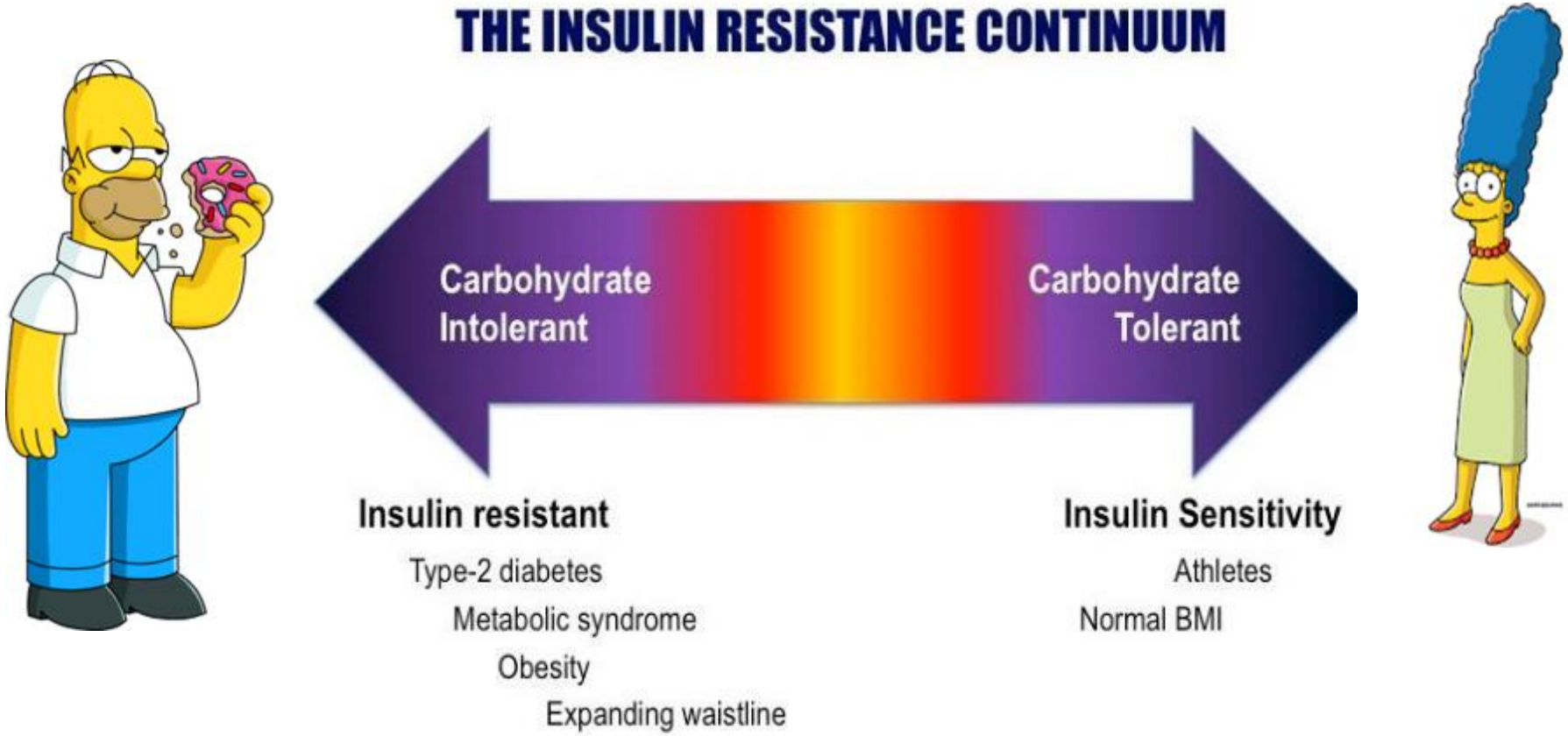


Figure 3 Dose–response relationship between physical activity and cardiovascular disease (CVD) mortality. Dose–response relation between metabolic equivalent of task (MET) min/week (with 750 MET min/week as the reference) and mortality risk estimated with restricted cubic spline regression and generalised least square trend estimation for summarised dose–response data.

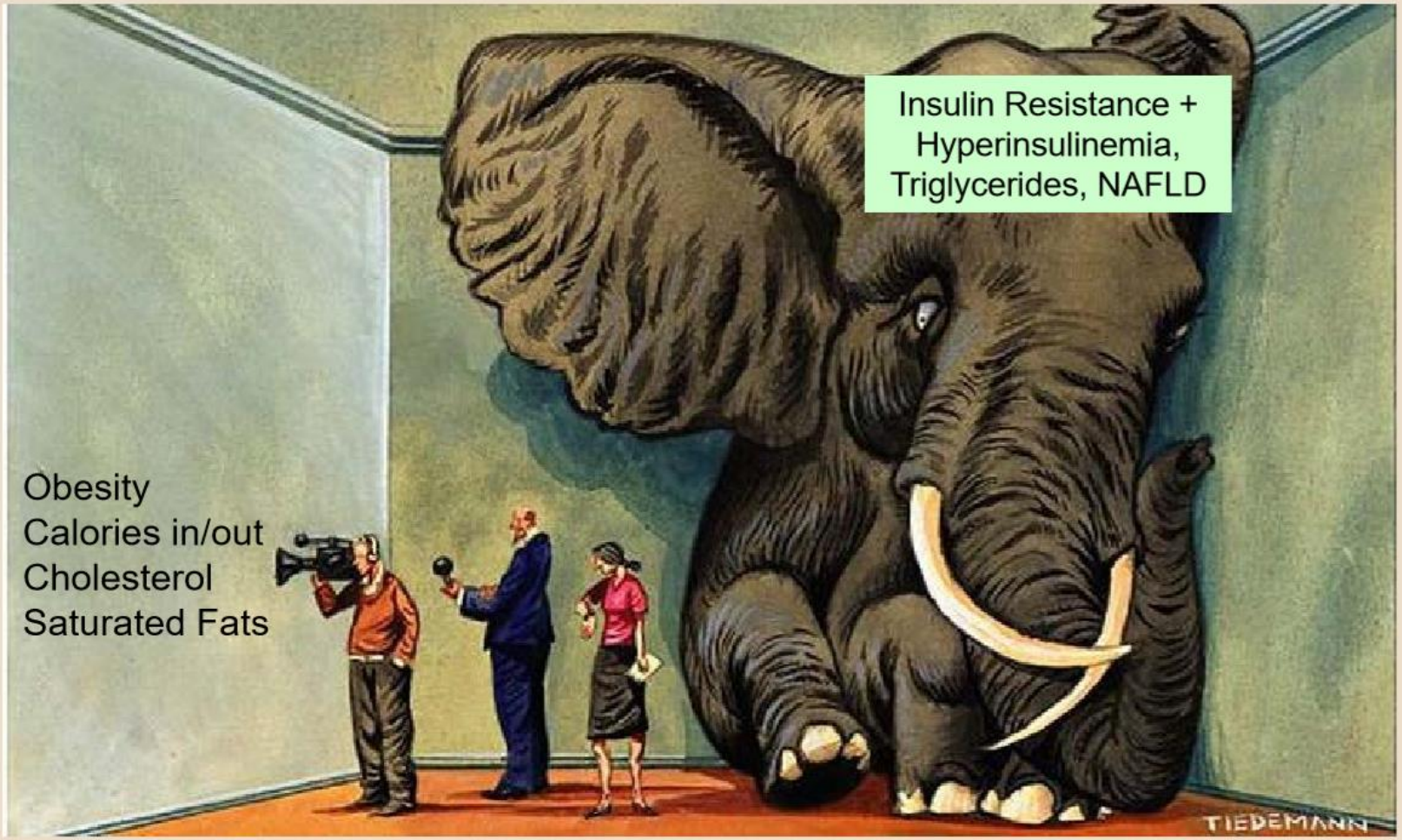


"What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?"

What Is The Phenotype Of Your Patient?

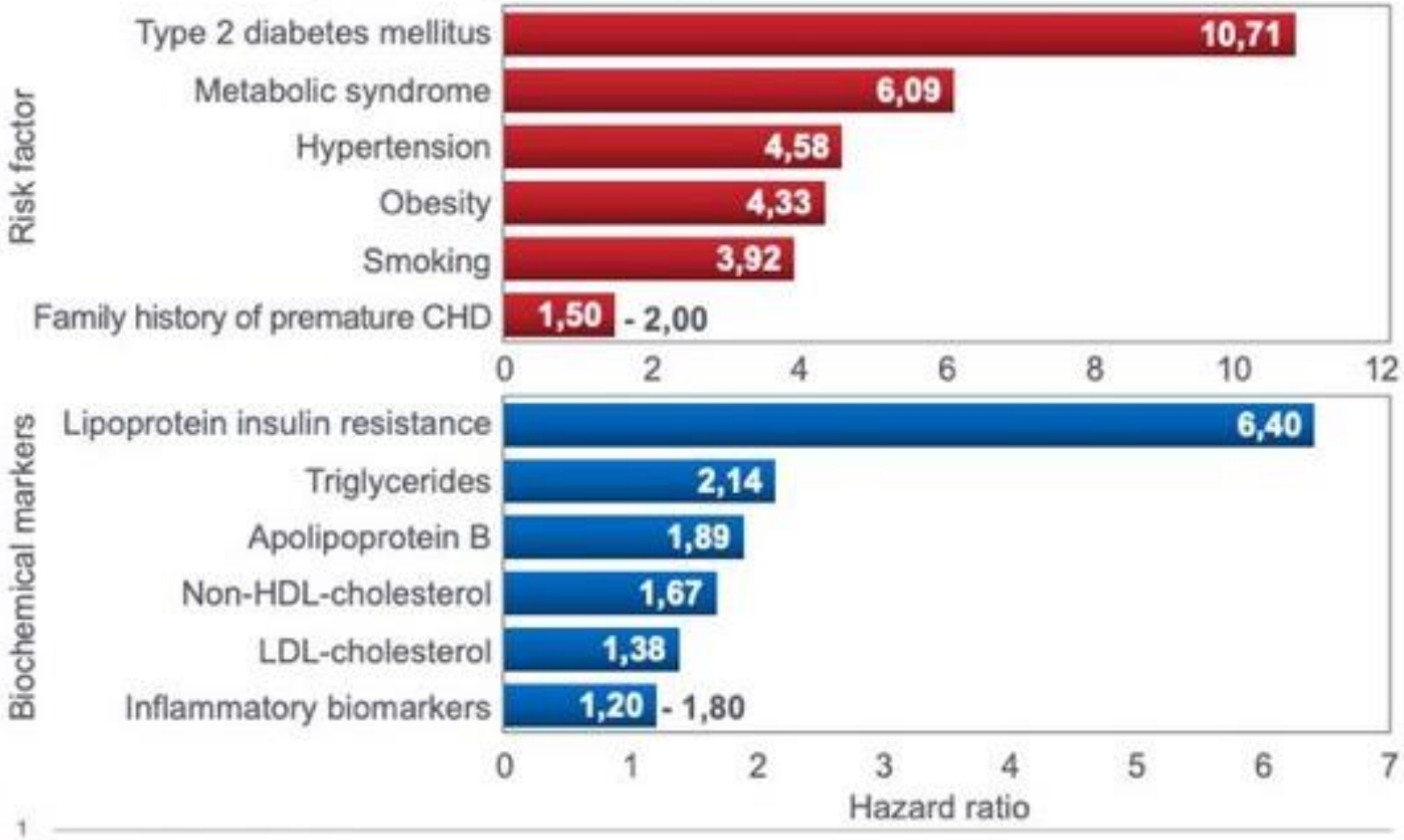


„The Elephant in the Room“



HAZARD RATIOS FOR DEVELOPMENT OF CORONARY HEART DISEASE – WOMEN'S HEALTH INITIATIVE

21.4 year Prospective Study - Women's Health Initiative



1

Association of Lipid, Inflammatory, and Metabolic Biomarkers With Age at Onset for Incident Coronary Heart Disease in Women
https://jamanetwork.com/journals/jamacardiology/fullarticle/2775559

Figure 1. Associations of Clinical Risk Factors and Lipid Biomarkers per SD Increment With Incident Coronary Heart Disease (CHD) by Age at CHD Onset

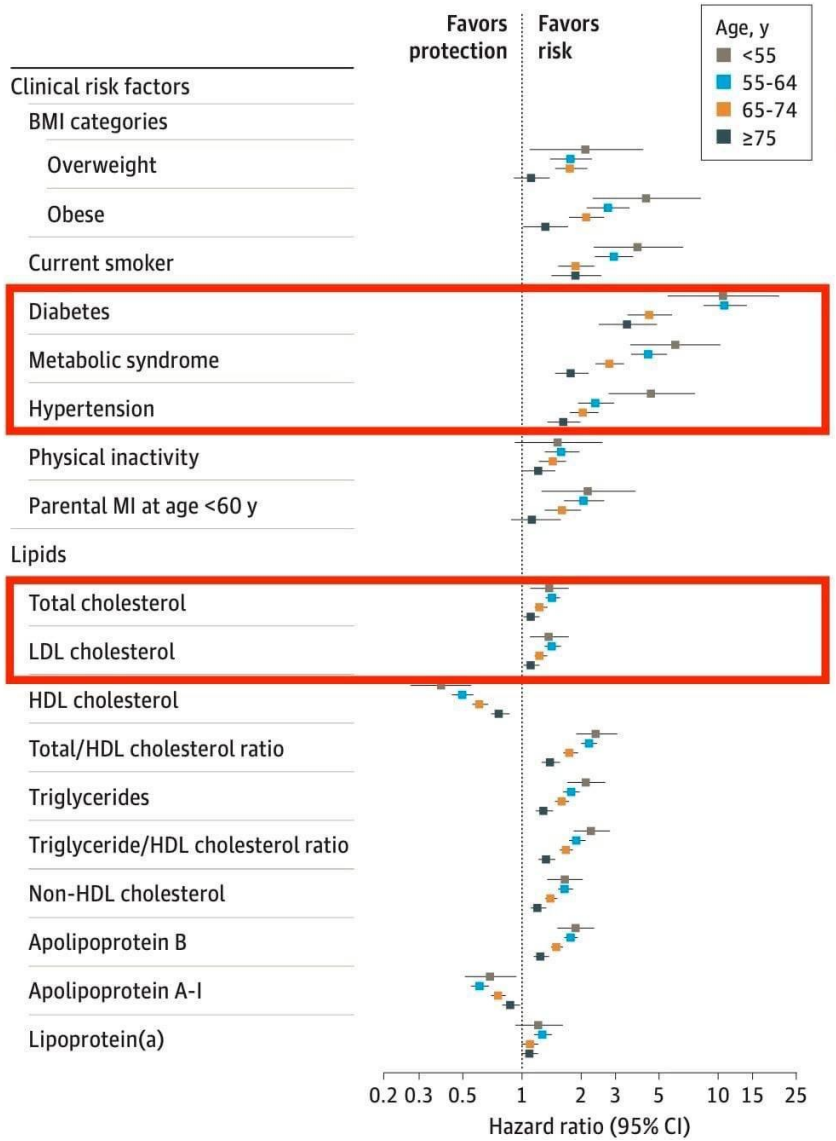
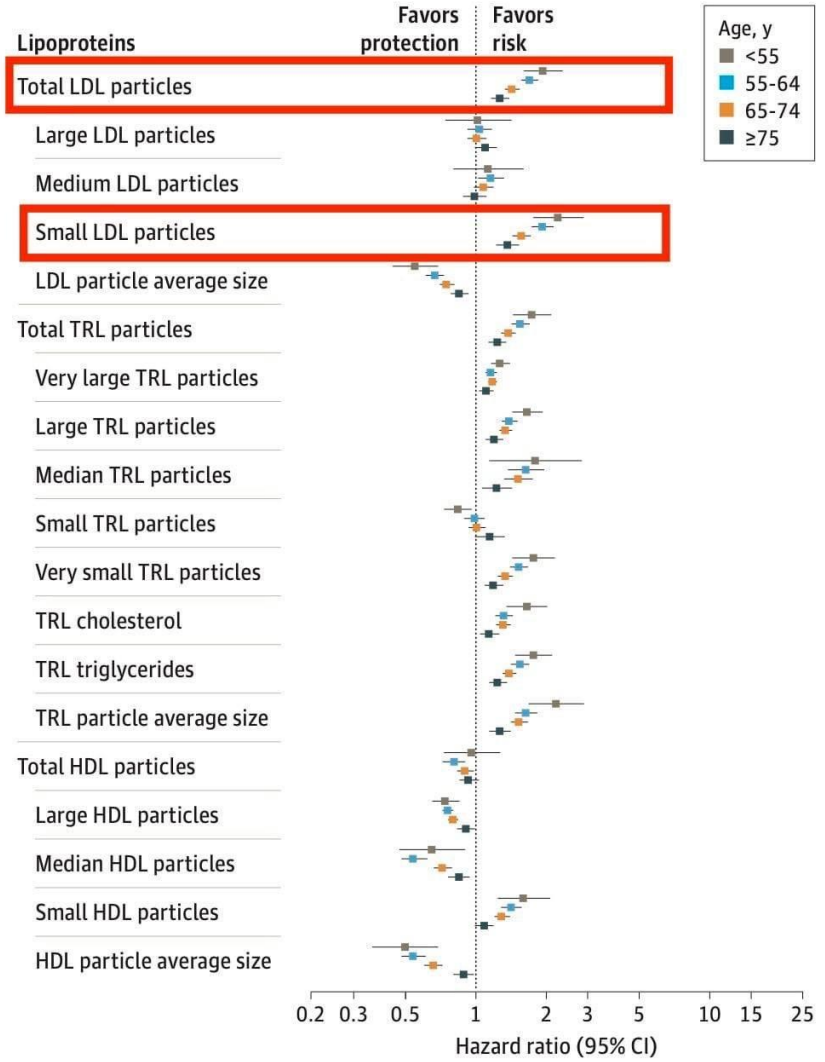


Figure 2. Associations of Lipoprotein Particles per SD Increment With Incident Coronary Heart Disease (CHD) by Age at CHD Onset for Low-Density Lipoprotein (LDL) Particles, Triglyceride-Rich Lipoprotein (TRL) Particles, and High-Density Lipoprotein (HDL) Particles



Why Is The World Not Talking About This?

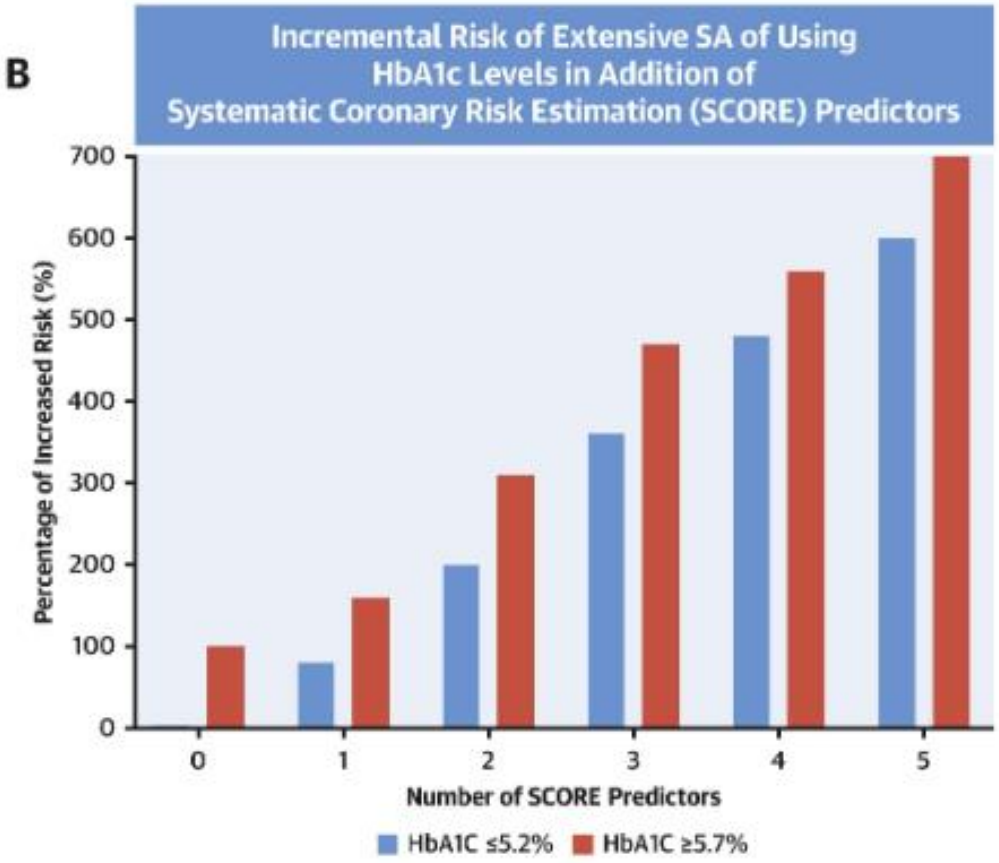
JAMA Cardiology | Original Investigation

Association of Lipid, Inflammatory, and Metabolic Biomarkers With Age at Onset for Incident Coronary Heart Disease in Women

Sagar B. Dugani, MD, PhD; M. Vinayaga Moorthy, PhD; Chunying Li, MPH; Olga V. Demler, PhD; Alawi A. Alsheikh-Ali, MD, MSc; Paul M Ridker, MD, MPH; Robert J. Glynn, PhD; Samia Mora, MD, MHS

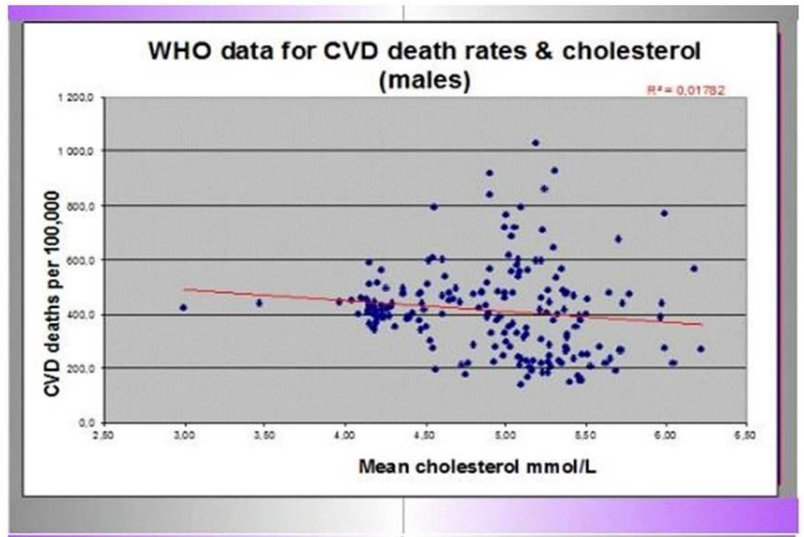
up to age 75 years. From approximately 50 biomarkers, lipoprotein insulin resistance had the highest standardized aHR: 6.40 (95% CI, 3.14-13.06) for CHD onset in women younger than 55 years, attenuating with age. In comparison, weaker but significant associations with CHD

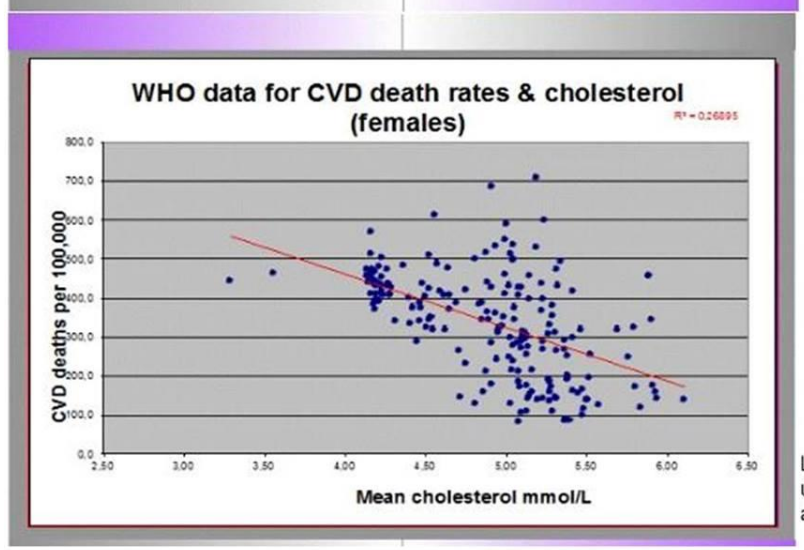
Glycated Hemoglobin and Subclinical Atherosclerosis in People Without Diabetes

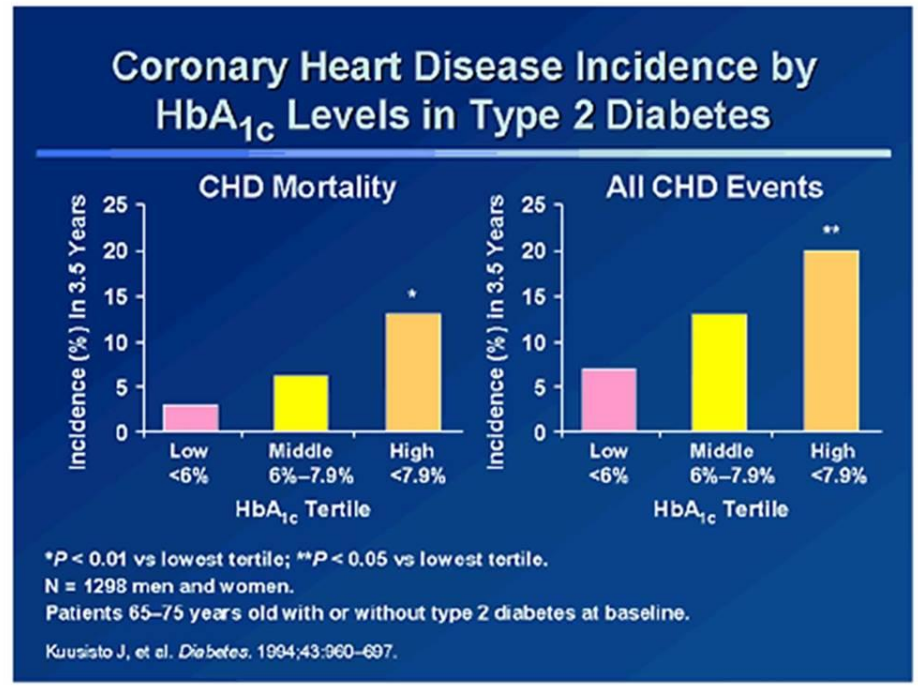


Rossello, X. et al. J Am Coll Cardiol. 2021;77(22):2777-91.

Worried about Heart Disease?
What's more important, cholesterol or A1c?







Cardiometabolic-Based Chronic Disease, Adiposity and Dysglycemia Drivers

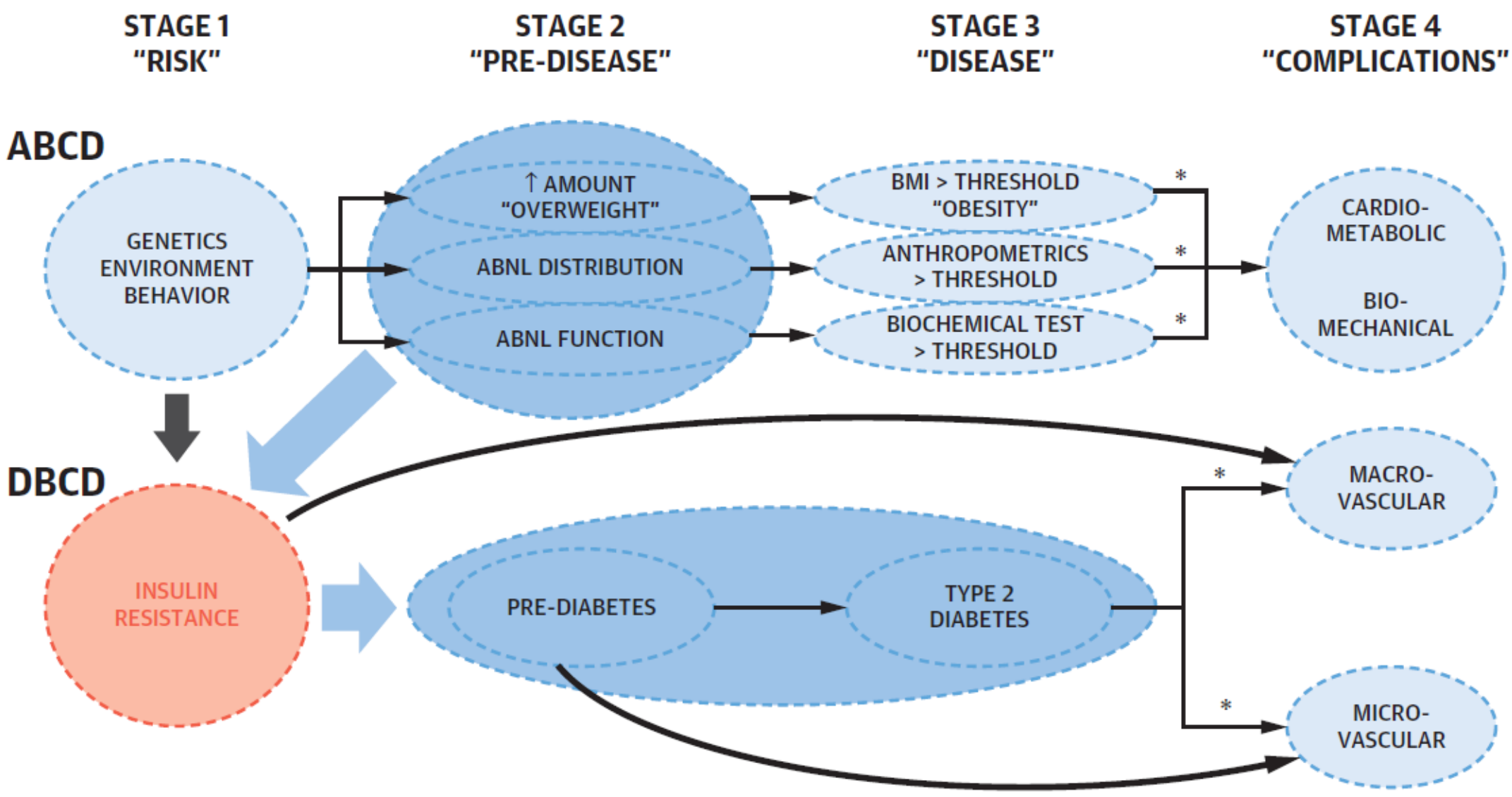
JACC State-of-the-Art Review

Jeffrey I. Mechanick, MD,[a] Michael E. Farkouh, MD, MSc,[b] Jonathan D. Newman, MD, MPH,[c]
W. Timothy Garvey, MD[d,e]

ABSTRACT

A new cardiometabolic-based chronic disease (CMBCD) model is presented that provides a basis for early and sustainable, evidence-based therapeutic targeting to promote cardiometabolic health and mitigate the development and ravages of cardiovascular disease. In the first part of this *JACC* State-of-the-Art Review, a framework is presented for CMBCD,

FIGURE 2 Insulin Resistance at the Intersection of ABCD and DBCD



Shaded areas and arrows indicate main causal relationships: abnormal adiposity to insulin resistance to dysglycemia. **Asterisks** indicate exertions of other metabolic syndrome traits. ABCD = adiposity-based chronic disease; ABNL = abnormal; BMI = body mass index; DBCD = dysglycemia-based chronic disease.

What the H is the Metabolic Syndrome?

- High BP
- Low HDL (<40 for Men <50 for Women)
- High Triglyceride (>150)
- Apple Belly
- High Glucose (Fasting Glucose >100)

- It's a Bad Weed
- Treat the Branches or the Root?

What is INSULIN RESISTANCE?

Chronically elevated levels of insulin over an extended period of time (years/decades) that results in the inability of insulin to properly function in the body contributing to disease.

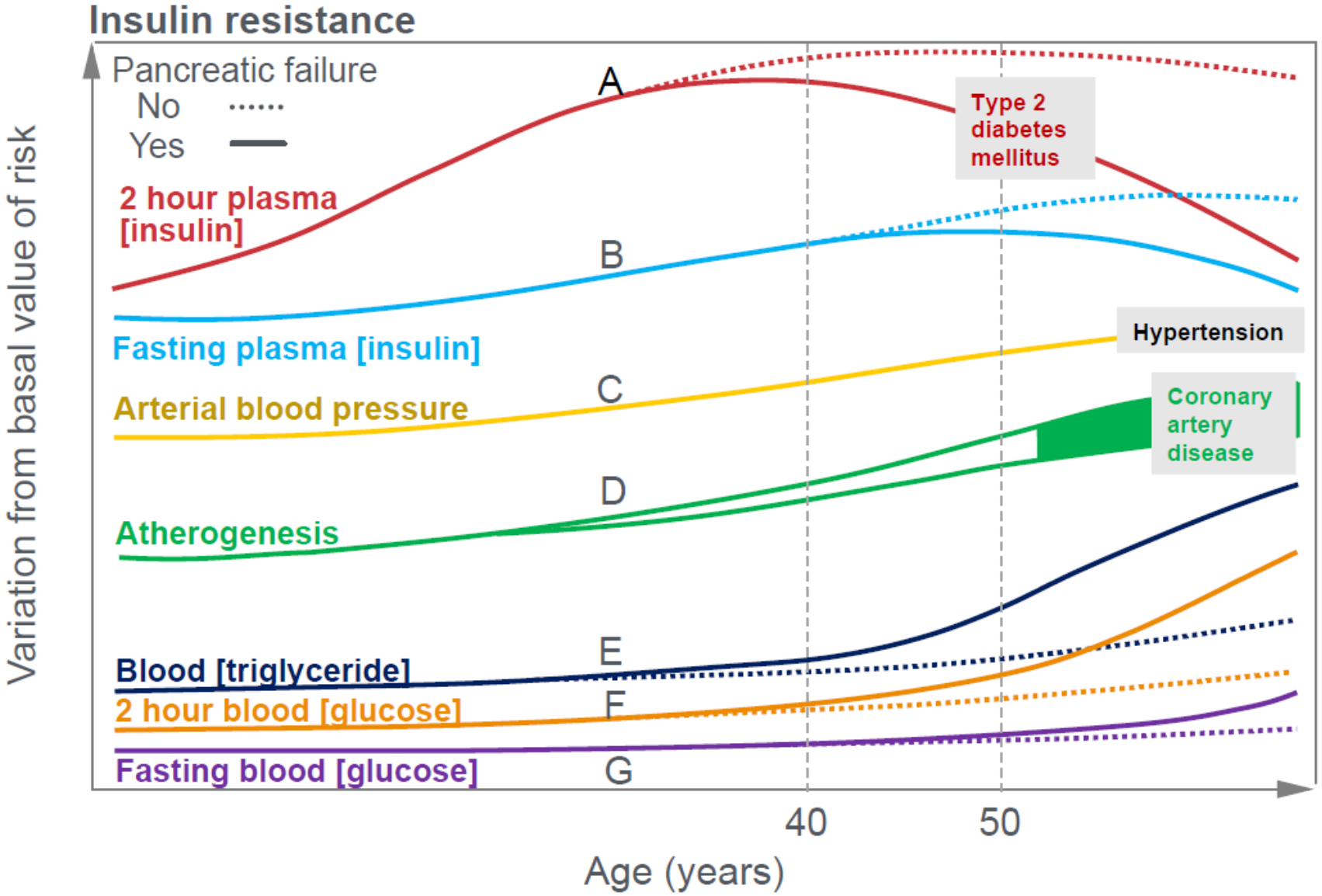

Heart Disease
Diabetes
Cancer
Body Fat
Fatty Liver
Insulin Resistance
Dementia
PCOS
Glucose
Insulin
Stroke
Sarcopenia
Arthriti
Migraines

Dr Ben Bikeman- Insulin IQ

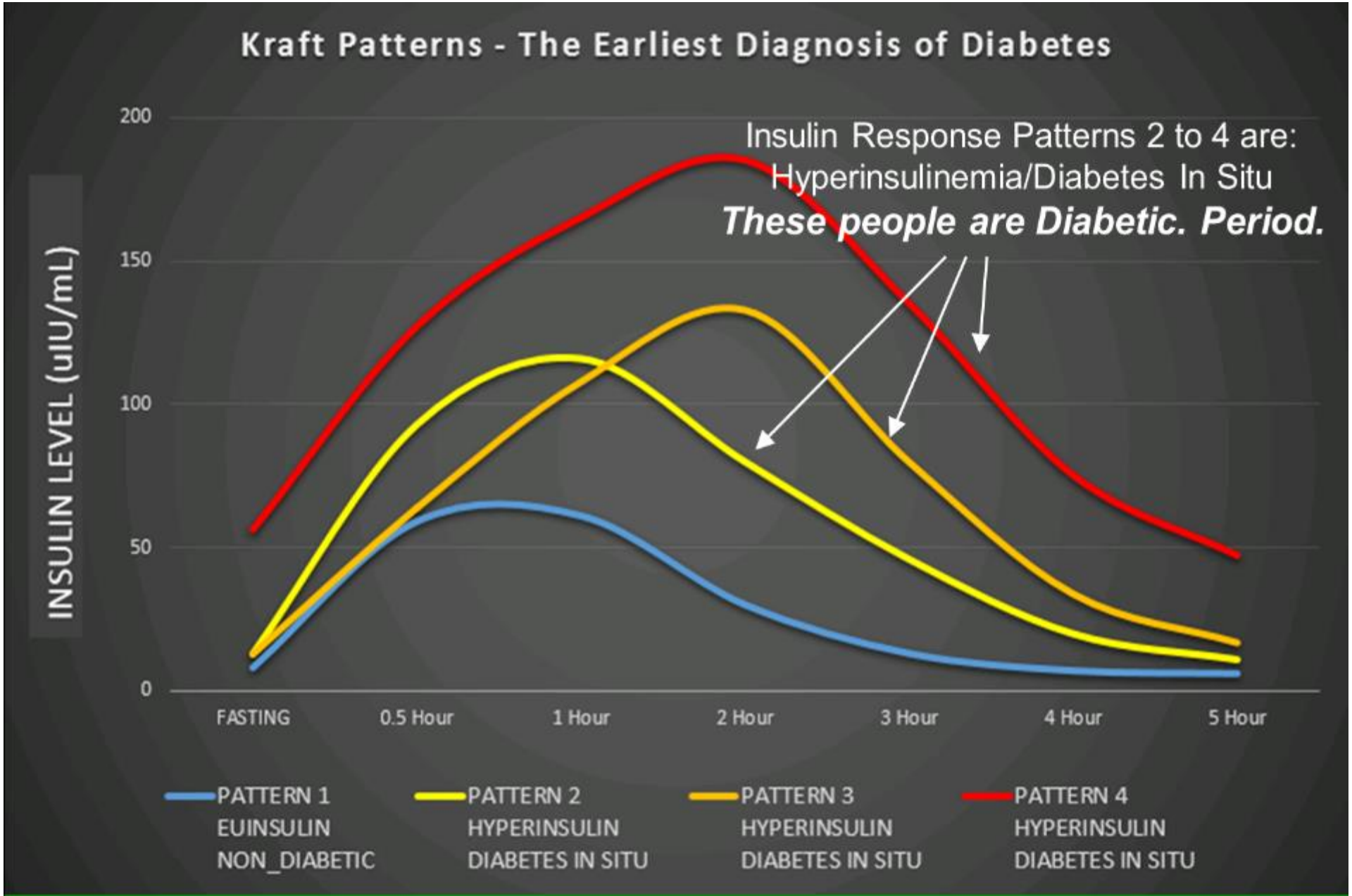
"You can almost throw a dart at a board of the most common chronic (and not-so-chronic) diseases and disorders and it's very likely ***Insulin Resistance*** *is either a leading cause or makes the disease worse."*

Nobody dies from Insulin Resistance— it's simply a vehicle that gets you there.

Proposed Time Sequence For The Development Of Progressive Hyperinsulinemia Leading To T2D, Coronary Artery Disease And HTN

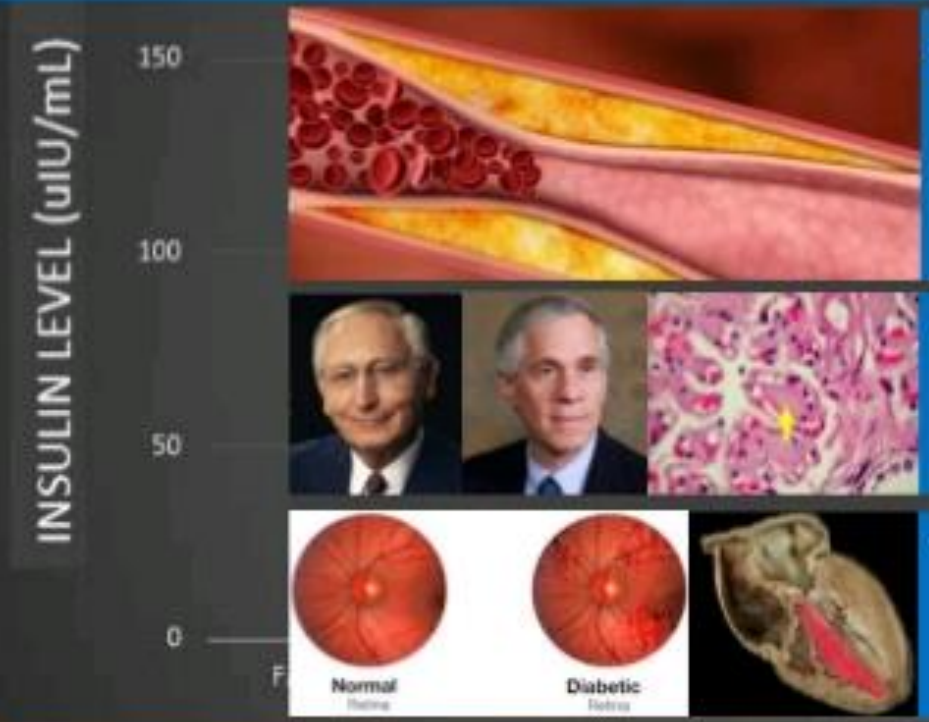


Kraft Patterns- Diabetes in Situ



Kraft Patterns - The Earliest Diagnosis of Diabetes

Critically, Kraft's research and >3,000 autopsies (personally conducted) led him to infer that:



- The damage of diabetes is vascular: ***you must assume diabetes is the root cause, unless Pattern 1 demonstrated!***
- The damage ***precedes*** the point where the glucose becomes elevated (ref: Kimmelsteil's work)
- This diabetic-driven disease is observed in all vessels, incl. micro vessels of the heart's IV Septum

In summary, Kraft concluded that:

"Those with cardiovascular disease not identified with diabetes…are simply undiagnosed."

….. Between 1999 and 2000 and 2017 and 2018, U.S. cardiometabolic health has been poor and worsening, with **only 6.8% of adults having optimal cardiometabolic health**

ELSEVIER

Journal of the American College of Cardiology

Volume 80, Issue 2, 12 July 2022, Pages 138-151

Original Investigation

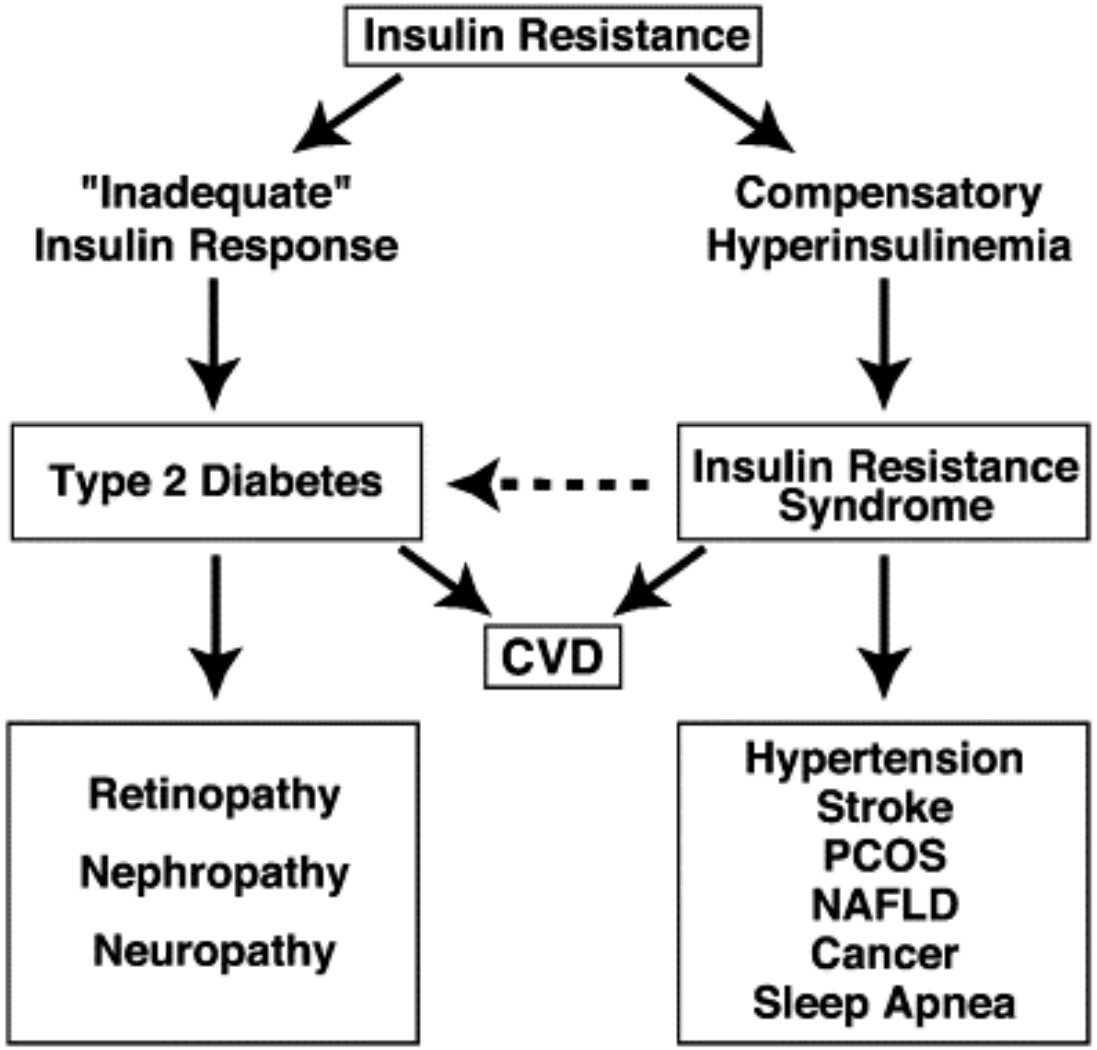
Trends and Disparities in Cardiometabolic Health Among U.S. Adults, 1999-2018

Meghan O'Hearn MS [a], Brianna N. Lauren MS [a], John B. Wong MD [b, c], David D. Kim PhD [c], Dariush Mozaffarian MD, DrPH [a, b]

Why Syndrome X? From Harold Himsworth to the Insulin Resistance Syndrome

Gerald M. Reaven*

Historical Perspective



Cell Metabolism 2005 1, 9-14DOI: (10.1016/j.cmet.2004.12.001)

Insulin Resistance- stuffing more (glucose) into the suitcase (cells) need more force (insulin)

Why Syndrome X? From Harold Himsworth to the Insulin Resistance Syndrome

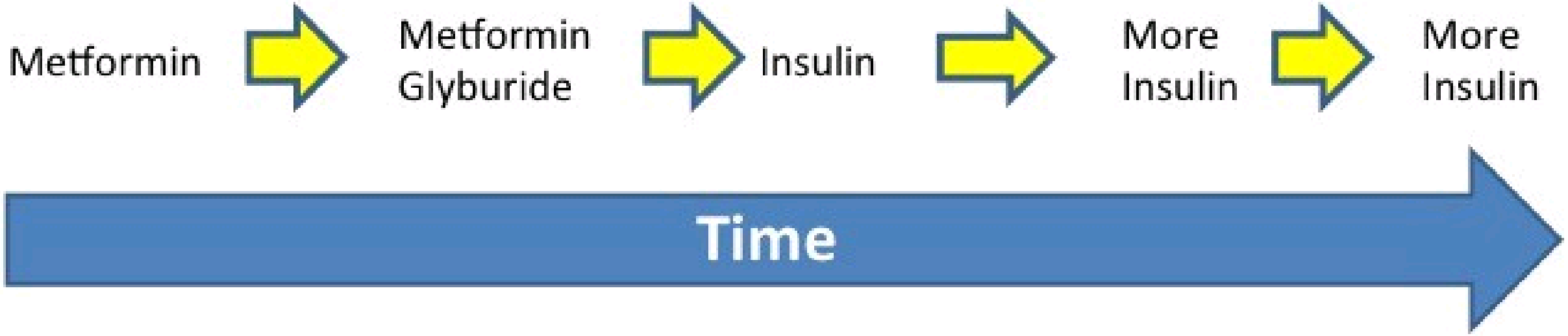
Historical Perspective

Gerald M. Reaven*

Clinical manifestations of insulin resistance
Type 2 diabetes
Essential hypertension
Cardiovascular disease
Polycystic ovary syndrome
Nonalcoholic fatty liver disease
Certain forms of cancer
Sleep apnea

CVD is getting worse!

Diabetes is getting worse!



Medications/insulin do not slow the march to CVD

- 7 multinational, multi-centre, randomized controlled trials of tight blood glucose control with medications (ACCORD, ADVANCE, VADT, ORIGIN, TECOS, ELIXA, SAVOR) failed to demonstrate reductions in heart disease, the major killer of diabetic patients.
- ***Using medications to lower blood sugar makes people healthier…maybe not true***

Association between prediabetes and risk of all cause mortality and cardiovascular disease: updated meta-analysis

Conclusions Results indicated that prediabetes was associated with an increased risk of all cause mortality and cardiovascular disease in the general population and in patients with atherosclerotic cardiovascular disease. Screening and appropriate management of prediabetes might contribute to primary and secondary prevention of cardiovascular disease.

BMJ 2020; 370 doi: https://doi.org/10.1136/bmj.m2297 (Published 15 July 2020)

Original Investigation | Nutrition, Obesity, and Exercise

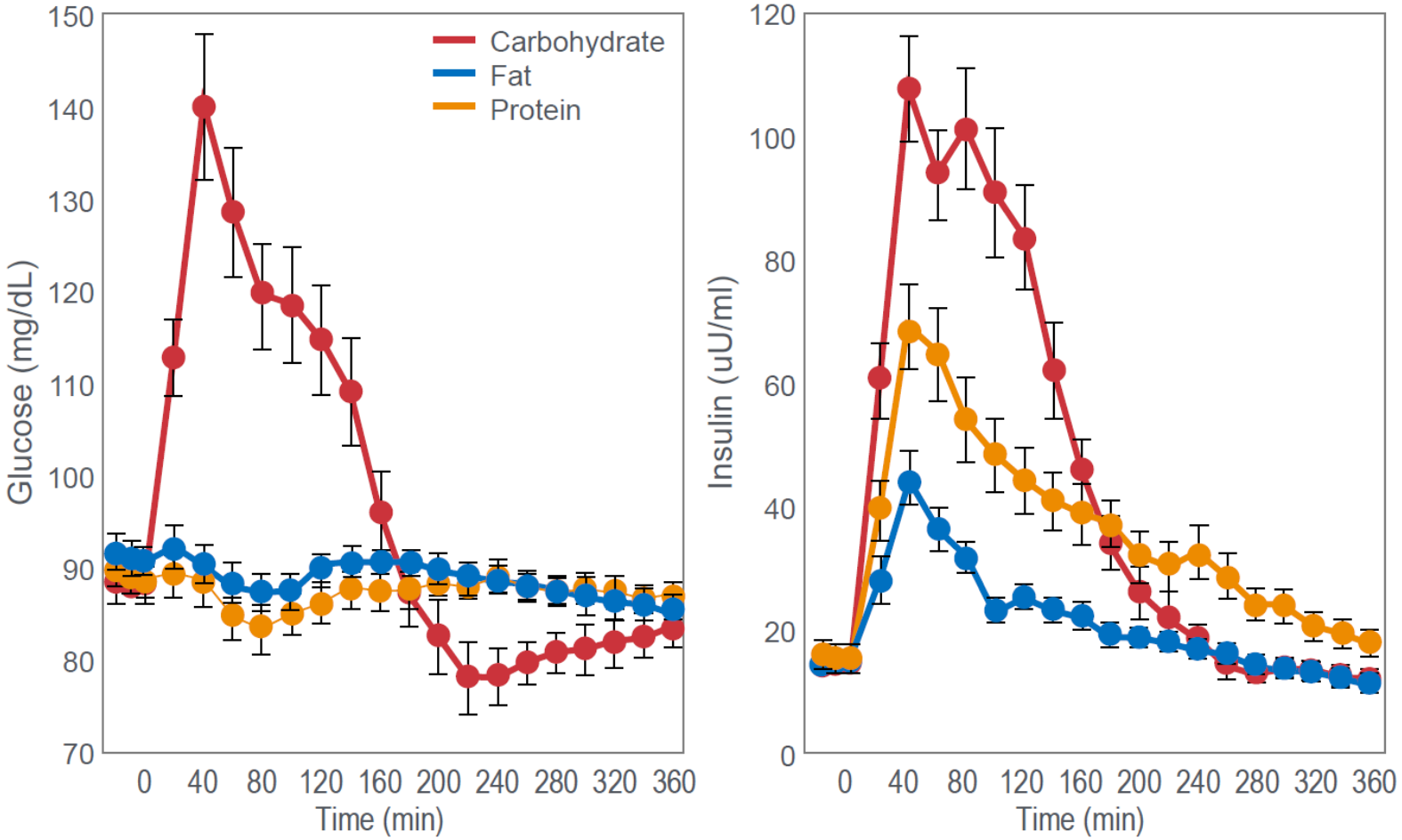
March 12, 2021

Temporal Associations Among Body Mass Index, Fasting Insulin, and Systemic Inflammation

A Systematic Review and Meta-analysis

The pooled evidence from this meta-analysis suggests that decreases in fasting insulin levels precede weight loss; it does not suggest that weight loss precedes decreases in fasting insulin. This temporal sequencing is not consistent with the assertion that obesity causes NCDs and premature death by increasing levels of fasting insulin. **This finding, together with the obesity paradox, suggests that hyperinsulinemia or another proximate factor may cause the adverse consequences currently attributed to obesity.** Additional studies to confirm this hypothesis are urgently needed.

Effects Of Carbohydrate, Fat Or Protein Ingestion On Plasma Glucose & Insulin Responses

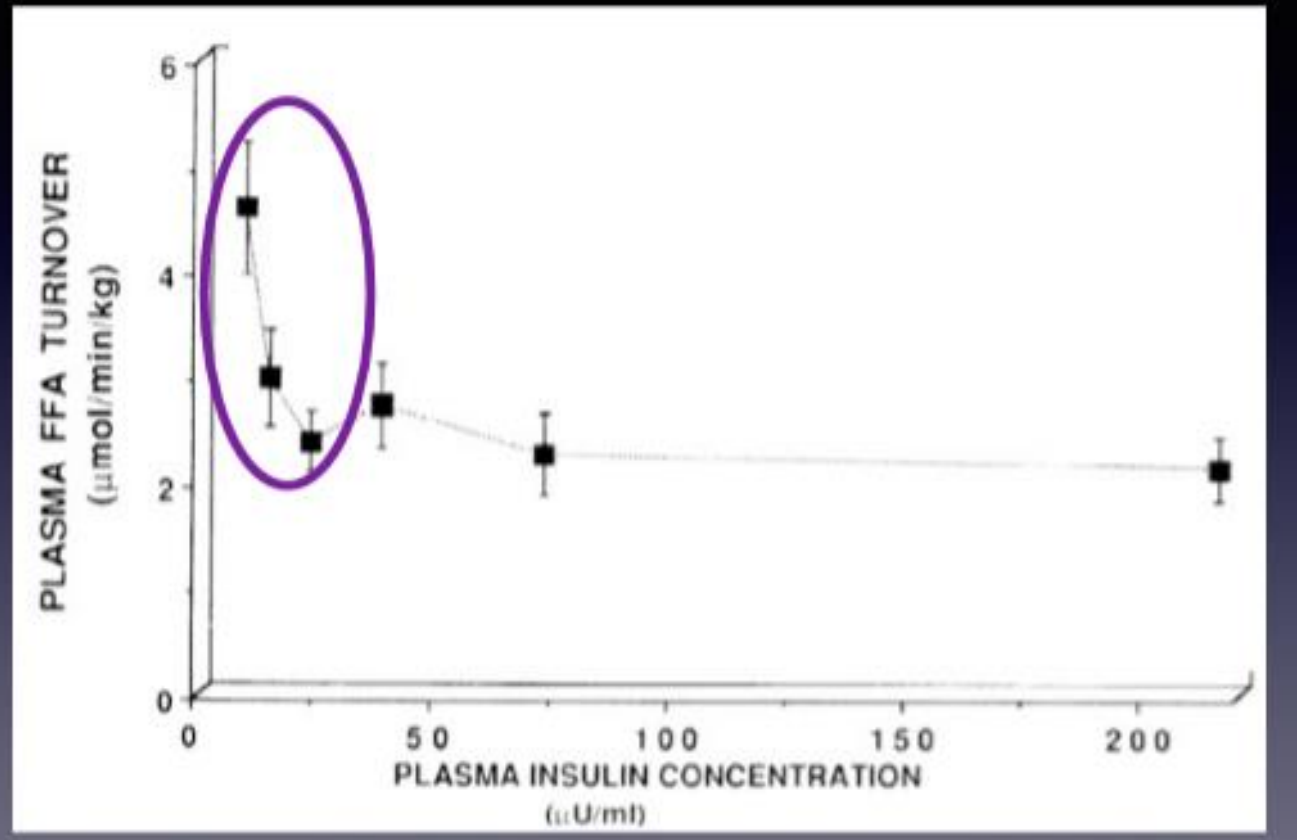


Foster-Schubert KE, Overduin J, Prudom CE, et al. *Clin Endocrinol Metab* 2008;93:1971-1979.

Minimizing insulin?

Release of fatty acids from fat cells "requires only the negative stimulus of insulin deficiency."

Rosalyn Yalow, Solomon Berson, 1965

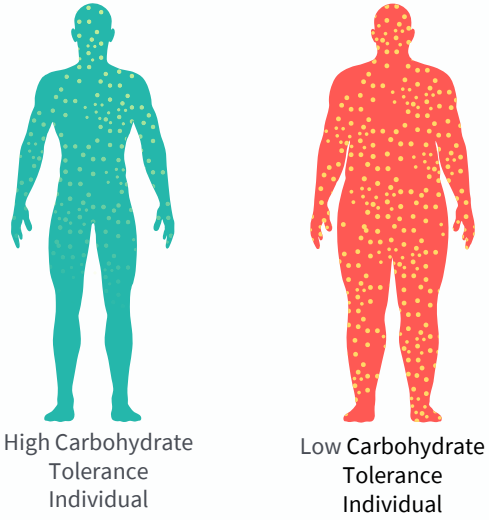


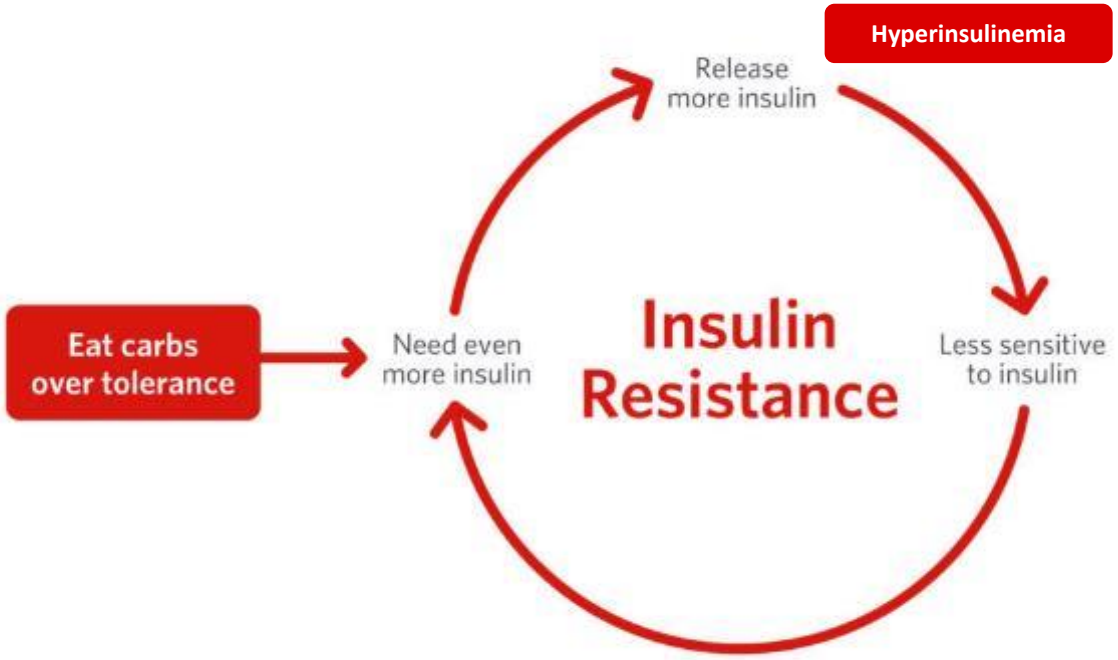
Bonadonna, 1991, Dose-dependent effect of insulin on plasma free fatty acid turnover and oxidation in humans

Insulin's Roles in Metabolism

- Regulating blood sugar to safe levels
- Regulating fuel storage or use of stored fuel

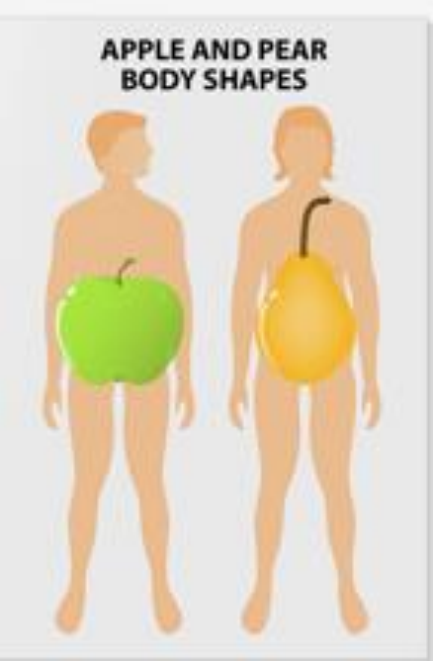
High Carbohydrate Diets Raise Insulin Levels and Increase Insulin Resistance. Carbohydrate Restriction Reverses this Trend.





Ludwig et al. Science 2018. 362:764
Page et al. Trends Endocrinology Metabolism 2018. 29:389

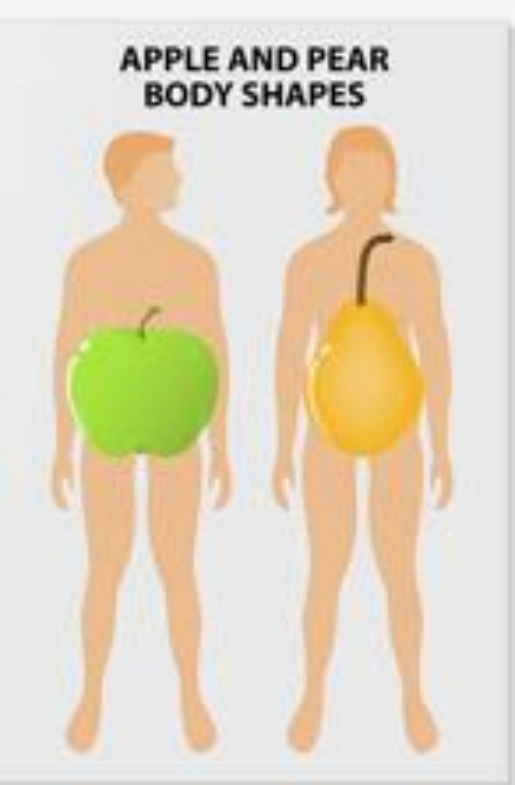
Pear vs Apple



- It matters hugely **where the fat is stored**.
- If the fat is stored under the skin, so called subcutaneous fat – **the wiggly bits** just below the skin particularly in the lower body at and below the hips including the buttocks and thighs – there appear to be **few adverse health consequences**.

Karpe F, Pinnick KE. Biology of upper-body and lower-body adipose tissuelink to whole-body phenotypes. *Nature Rev Endocrinol* 2015;11:90-100.

Pear vs Apple



- But the fat stored **above the hips** - within the abdomen especially **in the intra-abdominal organs** – the liver, pancreas and the intra-abdominal fat stores, so-called **visceral fat**, as well as **in skeletal muscles** - is harmful, especially once those cells become engorged with fat.

Zhang M, Hu T, Zhang S, et al. Associations of different adipose tissue depots with insulin resistance: A systematic review and meta-analysis of observational studies. *Nature Sci Reports* 2015;5:18495

PHYSIOLOGY

Comprehensive quantification of fuel use by the failing and nonfailing human heart

Danielle Murashige[1]*, Cholsoon Jang[2]*†, Michael Neinast[1]‡, Jonathan J. Edwards[3], Alexis Cowan[2], Matthew C. Hyman[4], Joshua D. Rabinowitz[2], David S. Frankel[4], Zolt Arany[1]§

The heart consumes circulating nutrients to fuel lifelong contraction, but a comprehensive mapping of human cardiac fuel use is lacking. We used metabolomics on blood from artery, coronary sinus, and femoral vein in 110 patients with or without heart failure to quantify the uptake and release of 277 metabolites, including all major nutrients, by the human heart and leg. The heart primarily consumed fatty acids and, unexpectedly, little glucose; secreted glutamine and other nitrogen-rich amino acids, indicating active protein breakdown, at a rate ~10 times that of the leg; and released intermediates of the tricarboxylic acid cycle, balancing anaplerosis from amino acid breakdown. Both heart and leg consumed ketones, glutamate, and acetate in direct proportionality to circulating levels, indicating that availability is a key driver for consumption of these substrates. The failing heart consumed more ketones and lactate and had higher rates of proteolysis. These data provide a comprehensive and quantitative picture of human cardiac fuel use.

Br J Sports Med
August 2017 Vol 51
No 15

Saturated fat does not clog the arteries: coronary heart disease is a chronic inflammatory condition, the risk of which can be effectively reduced from healthy lifestyle interventions

Aseem Malhotra,[1] Rita F Redberg,[2,3] Pascal Meier[4,5]

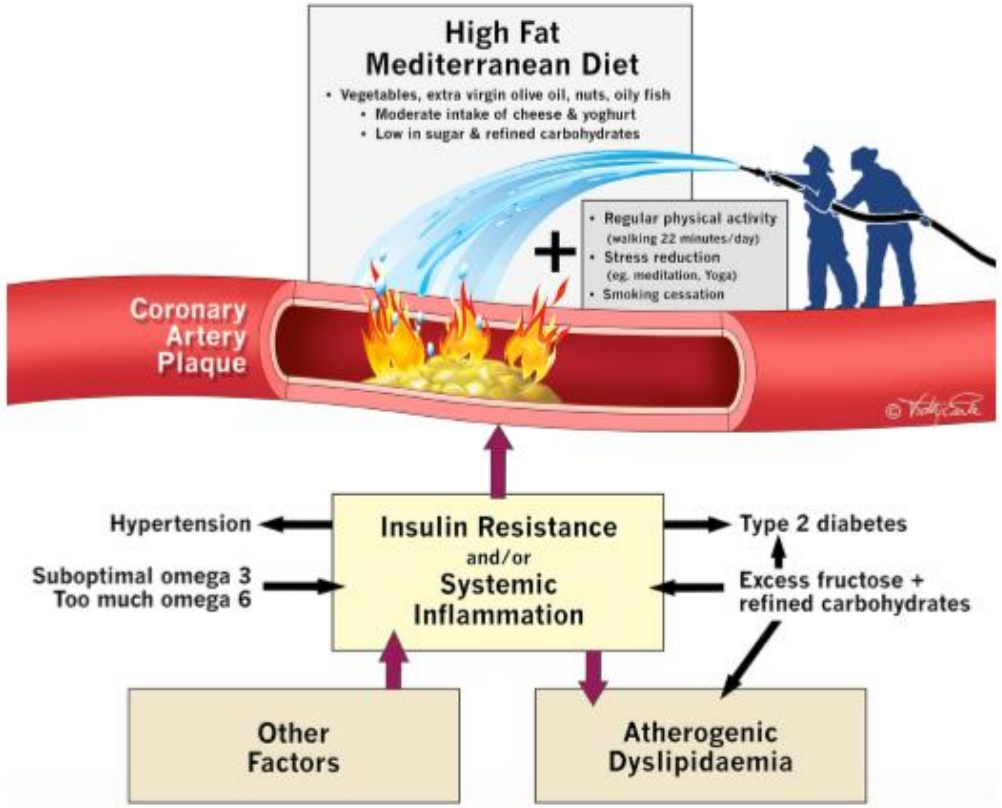
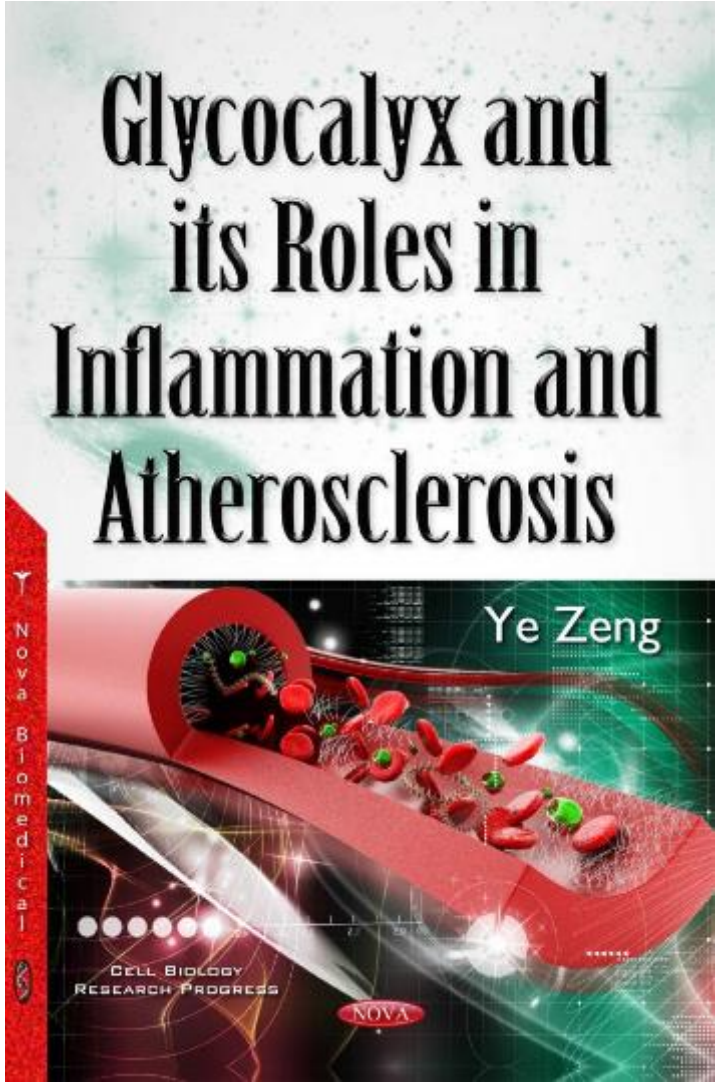
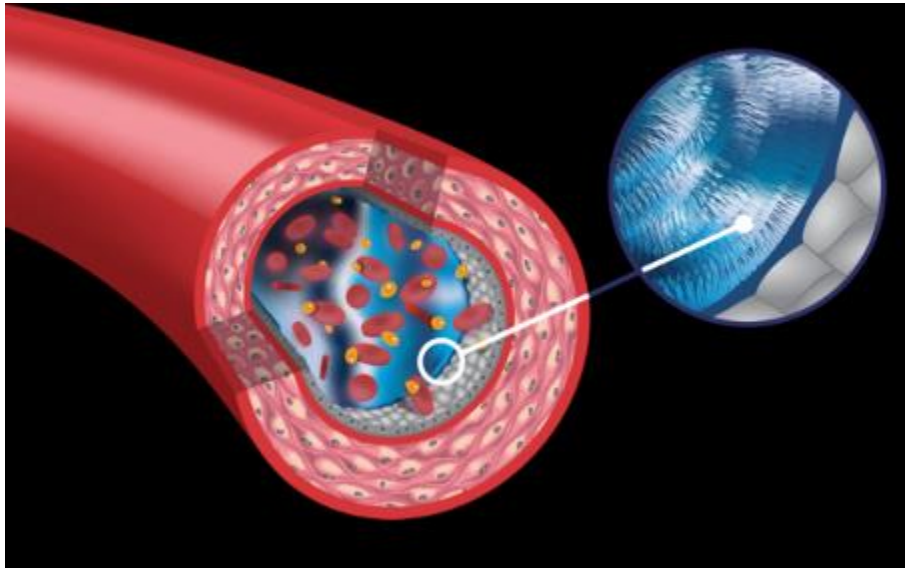


Figure 1 Lifestyle interventions for the prevention and treatment of coronary disease.



Glycocalyx
What injurs it?



Self-Assessment
Common Symptoms of Insulin Resistance

- Incremental abdominal fat accumulation over the years
- Overweight (Overfat)
- Elevated blood pressure (Hypertension)
- Elevated blood sugar markers (fasting blood glucose, Hemoglobin A1C)
- Disordered cholesterol markers (High LDL-C, High triglycerides, Low HDL-C)
- Family history of cardiovascular disease especially at a young age
- Family history of diabetes
- Family history of obesity

A Solution:
Fixing Metabolic Health

- ↑ Food Quality (Whole Foods)
- ↓ Carbohydrates and/or Carbohydrate frequency
- ↑ Dietary Fat (Fat Adaptation) Prioritize Protein
- ↑ Time between meals (IF/TRE)
- ↓ Stress / Cortisol
- ↑ Sleep
- ↑ Physical Activity

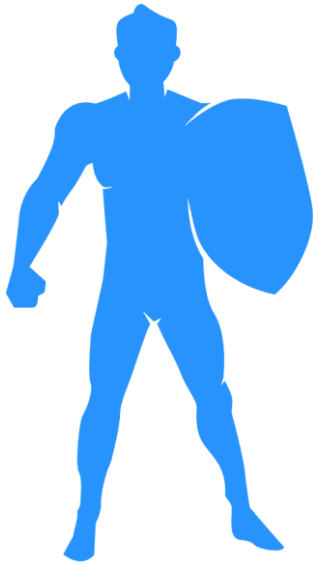
=

Low Insulin

Using Stored energy

↓

Burning Fat
Reducing Risk



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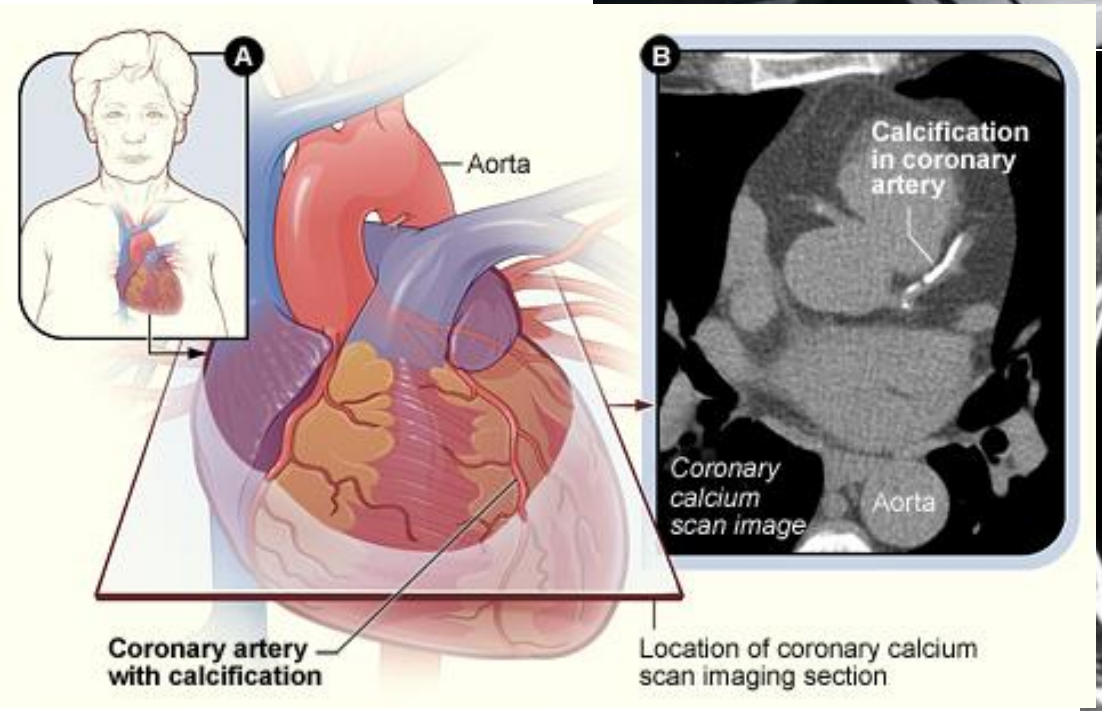
- ↓ Body Fat
- ↓ Blood Pressure
- ↓ Blood Sugars
- ↓ Inflammation
- Improved Blood Lipids
- ↑ Energy Levels
- ↑ Mental Clarity/Focus

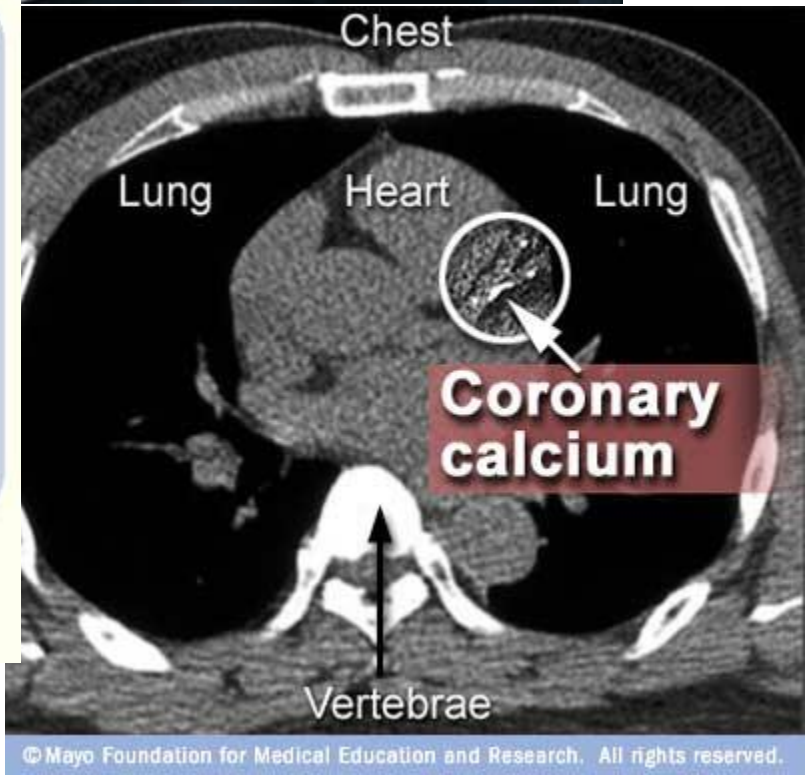
Take Aways

- ASCVD and Insulin Resistance is very common
- The good news this disease takes a really long time to occur
- The flip side of that is it takes a while to prevent
- Like moving towards an iceberg at slow speed from hundreds of miles away….you can’t wait until you’re looking at the iceberg to do anything about it.
- You want to be thinking about this through the lens of not 5 years worth of prevention, but 10, 20, 30 years of prevention

CAC Scores

~1 mSv





The CAC score – vital information

Table 2
Distribution of coronary artery calcium (CAC) scores by coronary heart disease (CHD) case status and associated odds ratio of coronary heart disease among all participants with coronary artery calcium scores in the Family Heart Study

	CAC Scores							
	0	1–49	50–99	100–199	200–399	400–999	1,000–1,999	2,000+
No. of cases	23 (5.9%)	23 (5.9%)	10 (2.6%)	20 (5.1%)	44 (11.3%)	88 (22.6%)	83 (21.3%)	98 (25.2%)
No. of non-cases	1,371 (46.2%)	799 (26.9%)	173 (5.8%)	173 (5.8%)	146 (4.9%)	190 (6.4%)	76 (2.6%)	42 (1.4%)
Odds ratio (univariate)	1.0	1.7	3.4	6.9	18.0	27.6	65.1	139
95% CI	—	0.96–3.1	1.6–7.4	3.7–12.8	10.5–30.6	17.0–44.7	38.8–109	80–241
p Value†	—	0.07	0.014	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Odds ratio (adjusted*)	1.0	1.2	2.0	3.8	9.4	12.5	28.5	55.7
95% CI	—	0.66–2.2	0.90–4.4	2.0–7.5	5.2–17.1	7.1–22.0	15.6–52.0	29.1–107
p Value†	—	0.55	0.089	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Adjustment for risk factors was performed using risk factors measured at the time of the coronary artery calcium scan in 2002 to 2004.

* Adjusted for age, gender, diabetes, hypertension, ever smoking, and high-density lipoprotein cholesterol (all risk factors significant; $p \leq 0.001$ before adding coronary artery calcium).

† Contrasting each category of coronary artery calcium scores to the 0 coronary calcium category.

.

Am J Cardiol. 2006 Jun 1;97(11):1564-9

Basic Res Cardiol (2014) 109:395
DOI 10.1007/s00395-013-0395-4

INVITED EDITORIAL

Time to quit that marathon running? Not quite yet!

Timothy Noakes

First, no cardiac events occurred during marathon races in line with the finding of low rates of sudden death or cardiac events during actual races. However, in four of seven runners who developed such events, some degree of physical activity triggered the event as we had noted previously [3]. The presence of premonitory symptoms that are frequently ignored may be an important factor explaining this relationship [3].

Second, 66 % of runners over 50 years of age were at low risk for a future cardiac event so that there would be no logical reason to dissuade them from their choice to continue marathon running.

Third, the presence of high CAC scores predicts increased risk for cardiac events. Thus runners with high CAC scores, with or without myocardial fibrosis, should be targeted for advice about the desirability of their continued marathon running.

BMJ Heart – CAC Paradox

https://heart.bmj.com/content/107/21/1710

Cardiac risk factors and prevention
Original research

PDF

Physical activity and the progression of coronary artery calcification

Ki-Chul Sung [1], Yun Soo Hong [2], Jong-Young Lee [1], Seung-Jae Lee [1], Yoosoo Chang [3, 4, 5], Seungho Ryu [3, 4, 5], Di Zhao [2], Juhee Cho [2, 4], Eliseo Guallar [2], Joao A C Lima [6]

Correspondence to Dr Ki-Chul Sung, Division of Cardiology, Department of Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul 03181, Korea (the Republic of); kcmd.sung@samsung.com; Dr Eliseo Guallar, Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD 21205, USA; eguallar@jhu.edu

- *Conclusion We found a positive, graded association between physical activity and the prevalence and the progression of CAC, regardless of baseline CAC scores.*

ORIGINAL RESEARCH ARTICLE

Relationship Between Lifelong Exercise Volume and Coronary Atherosclerosis in Athletes

CONCLUSIONS:

Participants in the >2000 MET-min/wk group had a higher prevalence of CAC and atherosclerotic plaques.

The most active group had a **more benign composition of plaques**

These observations may explain the **increased longevity typical of endurance athletes despite the presence of more coronary atherosclerotic plaque** in the most active participants.

Circulation. 2017;136:138–148. DOI: 10.1161/CIRCULATIONAHA.117.027834

SPECIAL ARTICLE ARCHIVE

Half a Century of Running — Clinical, Physiologic and Autopsy Findings in the Case of Clarence DeMar (Mr. Marathon)

James H. Currens, M.D.†, and Paul D. White, M.D.‡

- The New England Journal of Medicine in 1961, found that the Olympic marathoner and seven-time Boston winner--who'd been advised not to run due to a heart murmur--had coronary arteries "two to three times the normal diameter." These wide passageways allowed blood to flow freely even where DeMar had some blockage, and the results encouraged other fitness-minded physicians to pursue similar work relating fitness to heart health

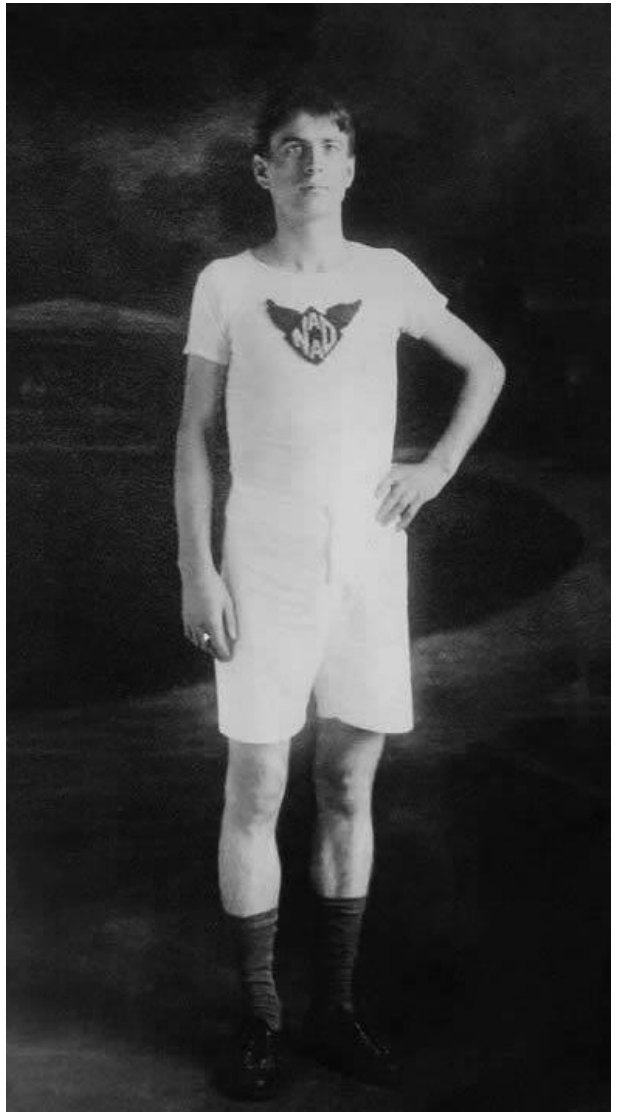


FIGURE 5. *Left Main Coronary Artery 0.5 Cm. from the Ostium in C.D., Showing a Fair Degree of Atherosclerosis of the Wall but Still with a Good-Sized Lumen.*

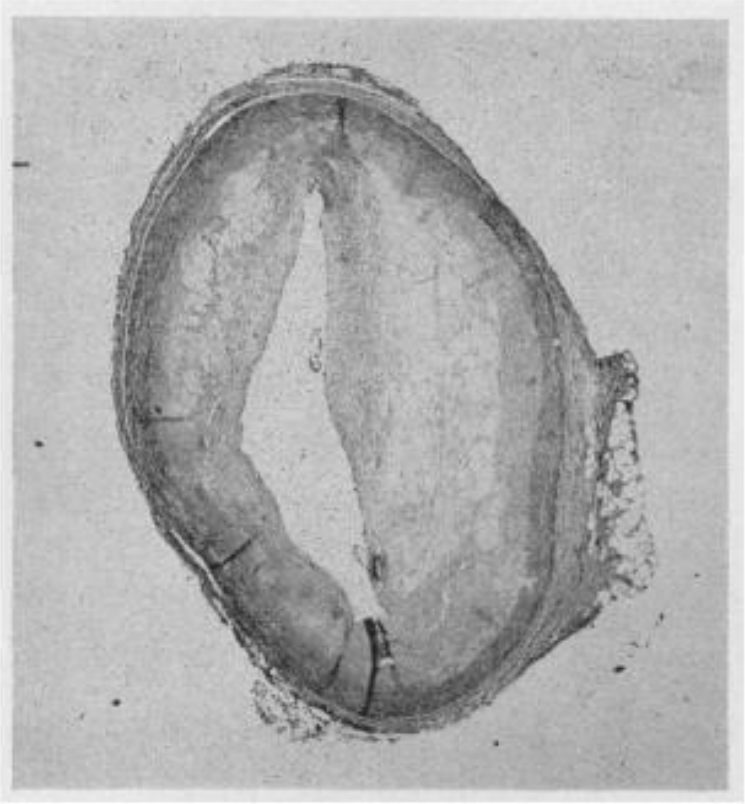


FIGURE 6. *Main Left Coronary Artery 0.5 Cm. from the Ostium in a "Control" Patient, Seventy Years of Age, Who Died from Cancer.*

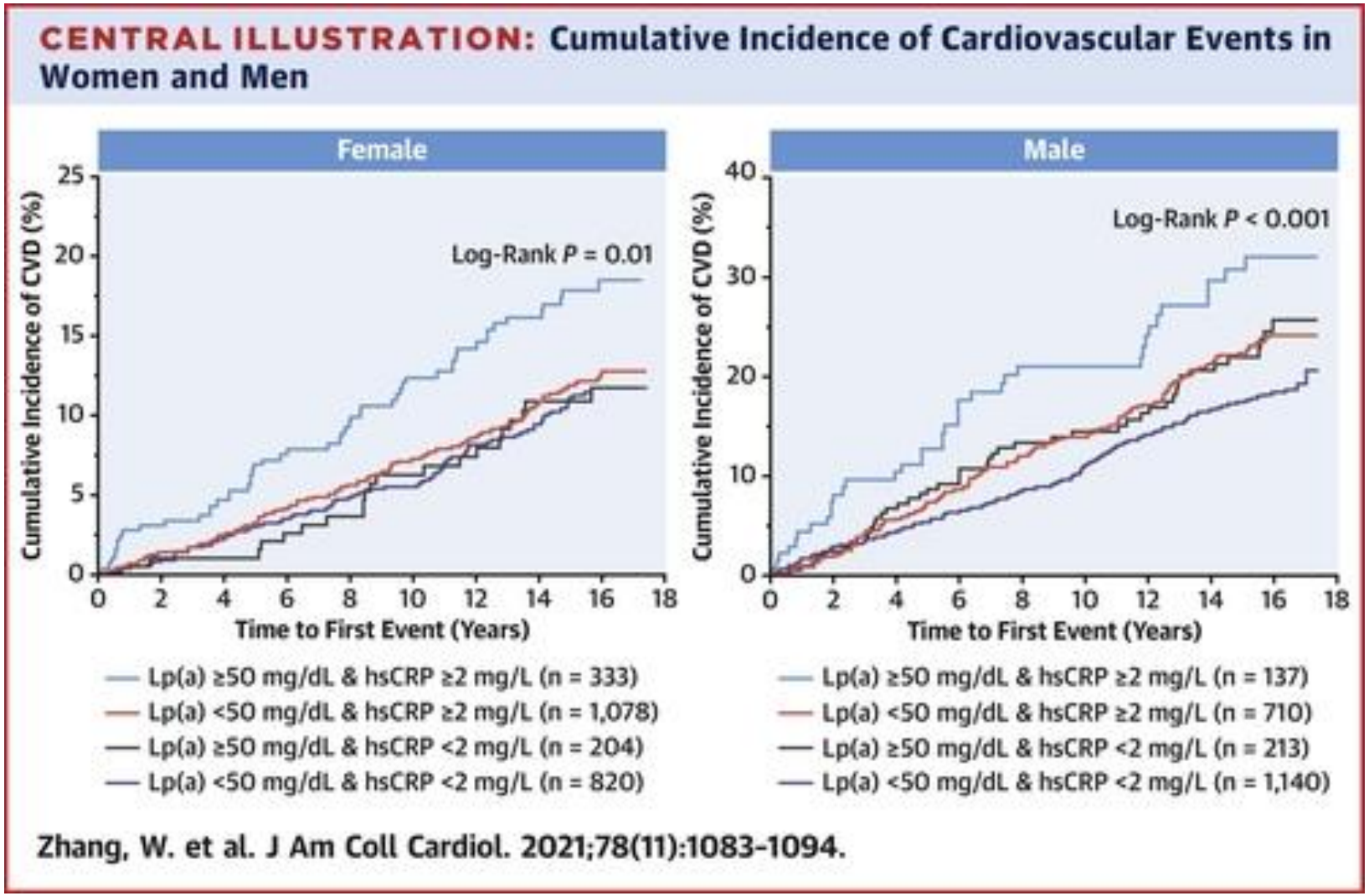
There was no clinical history of coronary heart disease, but a high degree of atherosclerotic narrowing of the lumen is apparent.

Put Your Own Oxygen Mask on
My Coronary Calcium 2022…..whew

FINDINGS:
Calcium scoring:
LM: 0.0
LAD: 0.0
Cx: 0.0
RCA: 0.0

Total Agatston score is 0.0.

Lp(a)- genetic marker of concern



Zhang, W. et al. J Am Coll Cardiol. 2021;78(11):1083-1094.

Know Your ApoB

Invited Commentary

November 13, 2021

Apolipoprotein B vs Low-Density Lipoprotein Cholesterol and Non-High-Density Lipoprotein Cholesterol as the Primary Measure of Apolipoprotein B Lipoprotein-Related Risk

The Debate Is Over

Allan D. Sniderman, MD[1]; Ann Marie Navar, MD, PhD[1,2]; George Thanassoulis, MD[1]

» Author Affiliations

JAMA Cardiol. 2022;7(3):257-258. doi:10.1001/jamacardio.2021.5080

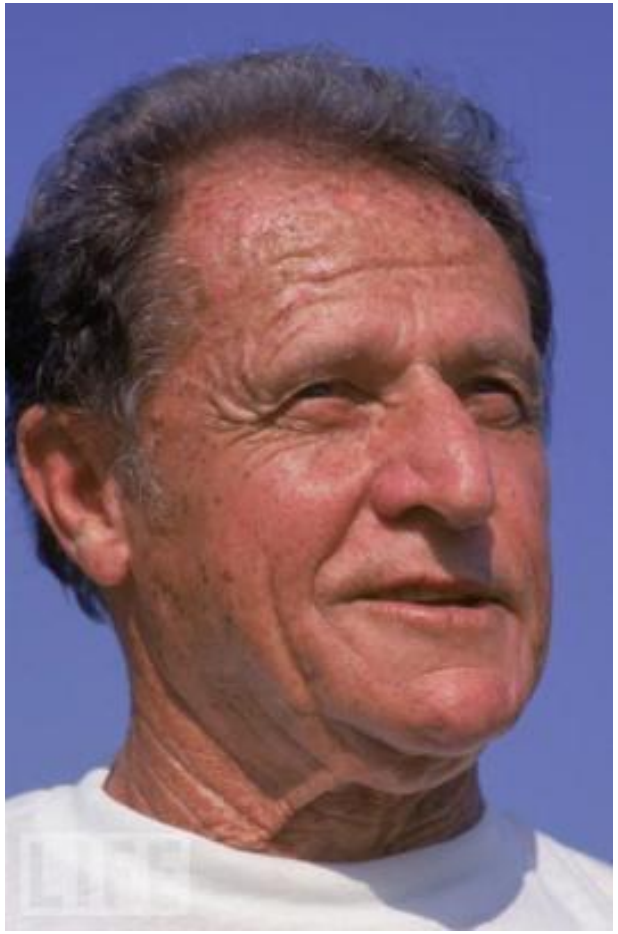
Exercise and Heart Attacks

- Moderate run will increase risk of a heart attack by 5 to 7 times vs sitting in a chair
- Heart attack lifetime risk 70% lower in most fit vs least fit
- “If your goal is to survive the next hour then go to bed- alone. But if your goal is to live a long healthy life then get some exercise for the next hour” Paul Thompson MD- Cardiologist

former NASA engineer Mary Shafer

“Insisting on perfect safety is for people who don’t have the balls to live in the real world.”

Understanding Aerobic



"Champions are everywhere; you just have to train them correctly."

The Founder of the Jogging Boom and Fitness for the Masses

President, Auckland Joggers Club 1962-2004

The first man to get Cardiac Patients Running

Andy
Steadman,
76 yrs,
3 coronaries

"the heart's just another muscle which needs to get fit with exercise"

The Man who Inspired Bill Bowerman

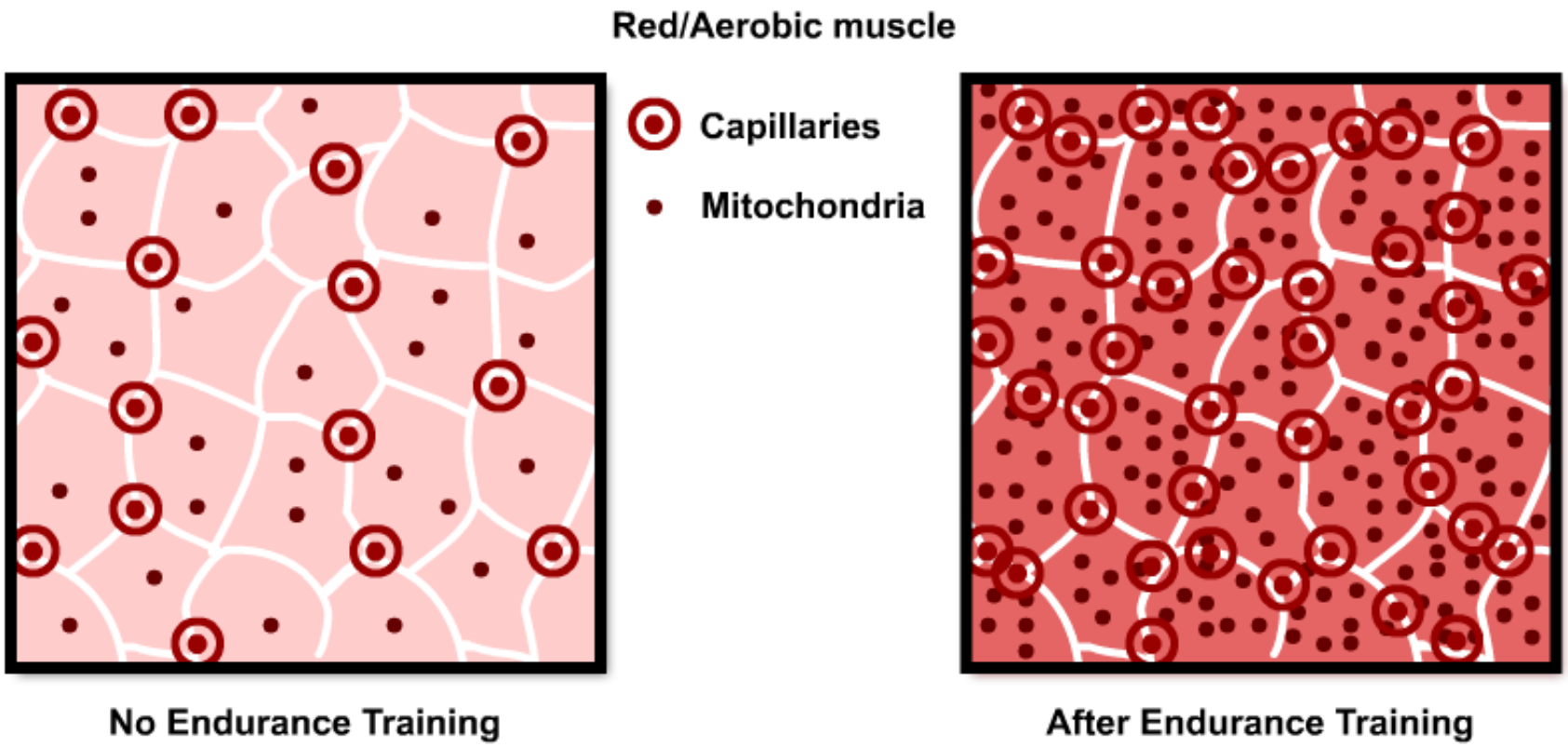
Who at 50, couldn’t keep up with the Lydiard-trained coronary patients

“If you have a body you are an athlete”….

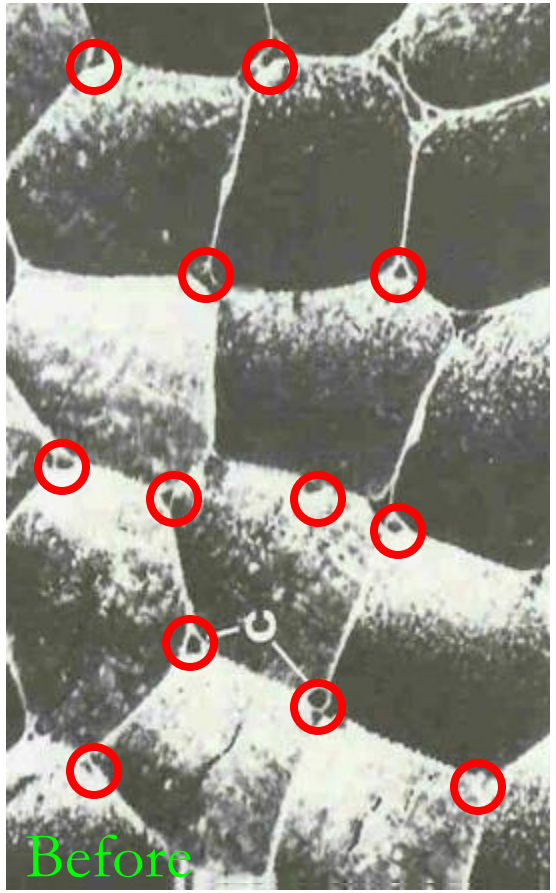
Bill Bowerman, Legendary Oregon Coach and co-founder of Nike

Invented *Jogging* for the masses

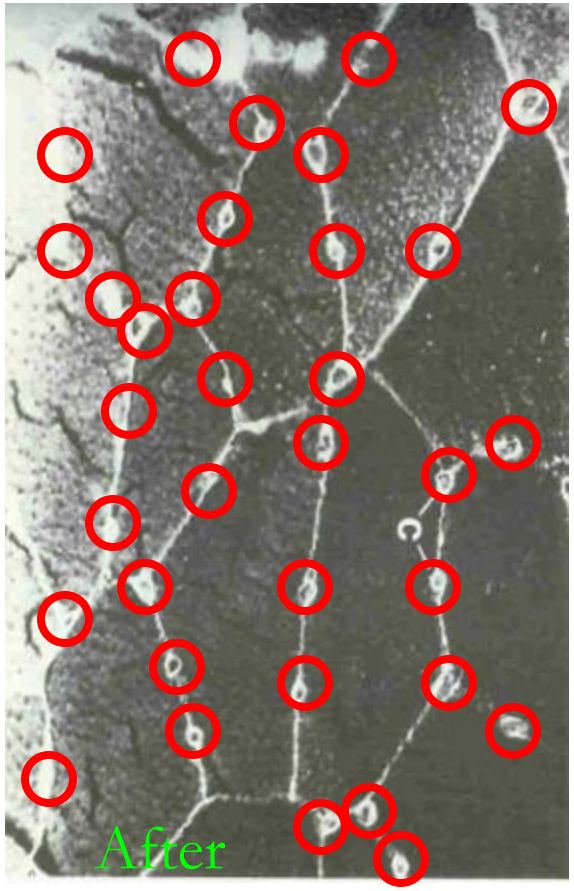
The Effect of Endurance Training



Building Capillaries and Mitochondria



Capillaries in muscles



After endurance training

(D.L. Costill; photo by L. Hermansen)

J. Physiol. (1979), **294**, *pp.* 419–432
Printed in Great Britain

EFFECTS OF ENDURANCE TRAINING ON MUSCLE FIBRE ATP-ASE ACTIVITY, CAPILLARY SUPPLY AND MITOCHONDRIAL CONTENT IN MAN

BY FRANK INGJER

From the Laboratory of Physiology, Norwegian College of Physical Education and Sport, Oslo, and Anatomical Institute, University of Oslo, Norway

(*Received 27 October 1978*)

nutrients

MDPI

Review

Glucose Uptake by Skeletal Muscle within the Contexts of Type 2 Diabetes and Exercise: An Integrated Approach

Nicholas A. Hulett [1], Rebecca L. Scalzo [1,2,3] and Jane E. B. Reusch [1,2,3,*]

[1] Department of Medicine, Anschutz Medical Campus, University of Colorado, Aurora, CO 80045, USA; nicholas.hulett@cuanschutz.edu (N.A.H.); rebecca.scalzo@cuanschutz.edu (R.L.S.)
[2] Rocky Mountain Regional Veterans Affairs Medical Center, Aurora, CO 80045, USA
[3] Center for Women's Health Research, Anschutz Medical Campus, University of Colorado, Aurora, CO 80045, USA
* Correspondence: jane.reusch@CUAnschutz.edu

Published: 14 October 2016

Exercise-stimulated glucose uptake – regulation and implications for glycaemic control

Lykke Sylow, Maximilian Kleinert, Erik A. Richter & Thomas E. Jensen

Nature Reviews Endocrinology **13**, 133–148 (2017) | Cite this article

Insulin Dependent and Independent Glucose Disposal

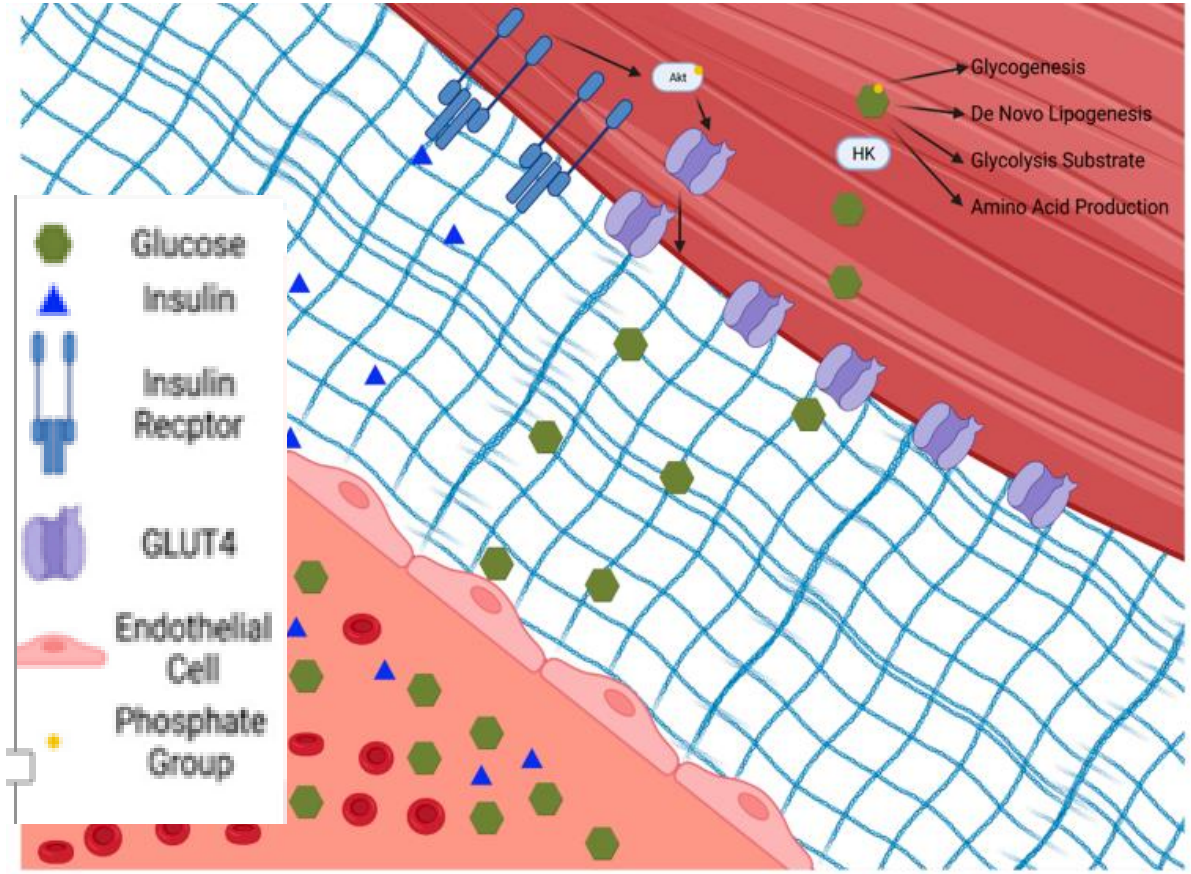


Figure 1. Insulin-dependent and -independent skeletal muscle glucose disposal requires: (1) glucose delivery to the muscle from circulation through the extracellular matrix to the cell membrane; (2) uptake via facilitative glucose transporters either constitutively on the cell membrane or translocated in response to insulin or exercise; and (3) a glucose diffusion gradient to drive glucose into the cell which is modulated by intracellular glucose metabolism. Hexokinase (HK). Phosphokinase B (Akt).

- How exercise mobilizes glucose transporters—an important factor in diabetic patients

T2D- Full System Disruption

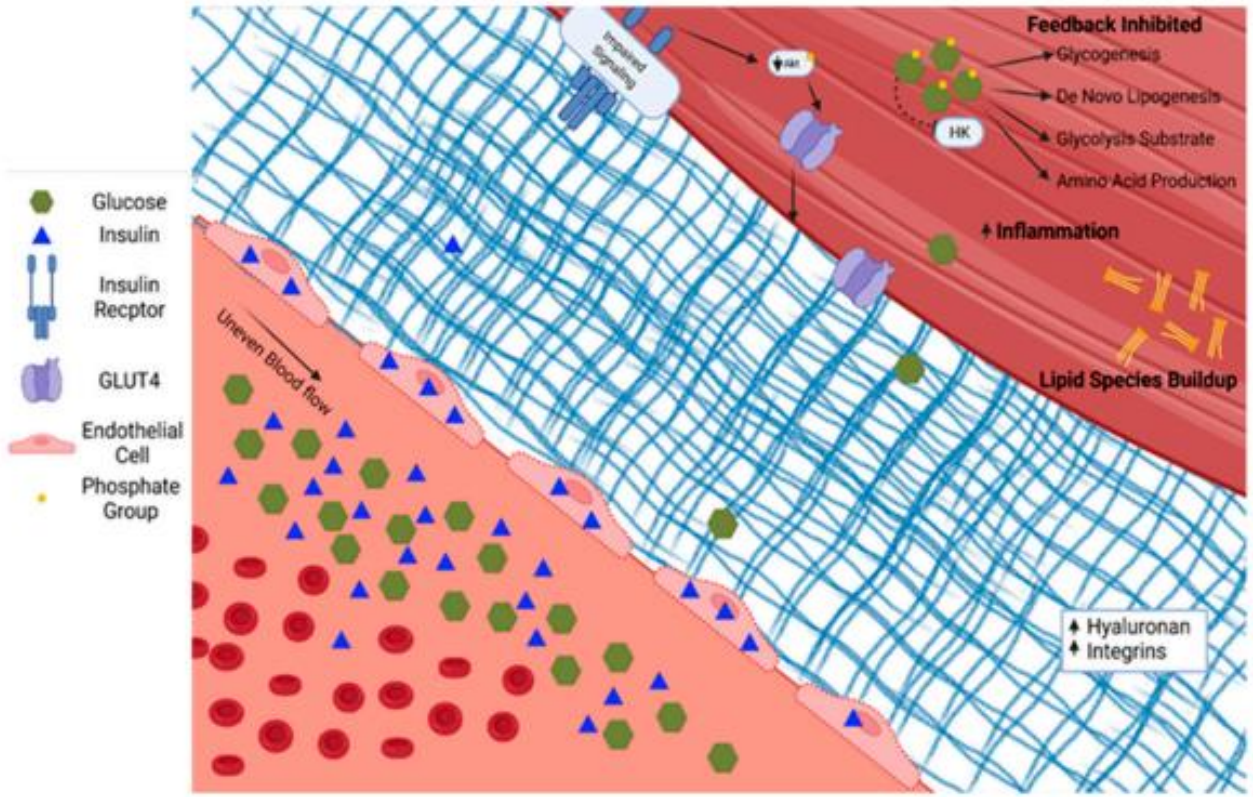


Figure 2. Type 2 diabetes is characterized by increased glucose and insulin in circulation. Insulin accumulates in endothelial cells. The extracellular matrix becomes fibrotic with increased hyaluronan and integrins. Serine/threonine phosphorylation on the insulin receptor and insulin response substrates leads to blunted insulin signaling through PI3K/Akt. The glucose diffusion gradient is limited by elevated intracellular glucose concentrations and allosteric down-regulation of intracellular glucose metabolism. Hexokinase (HK). Phosphokinase B (Akt).

- **With IR- difficulty translocating GLUT4 transporters** to the surface of the muscle- These move glucose into the cell
- **Skeletal muscle-** ? first tissue where diabetes starts- 80% of the carbohydrates oxidized in skeletal muscle. **50x glucose utilization w exercise**

Effects of Exercise

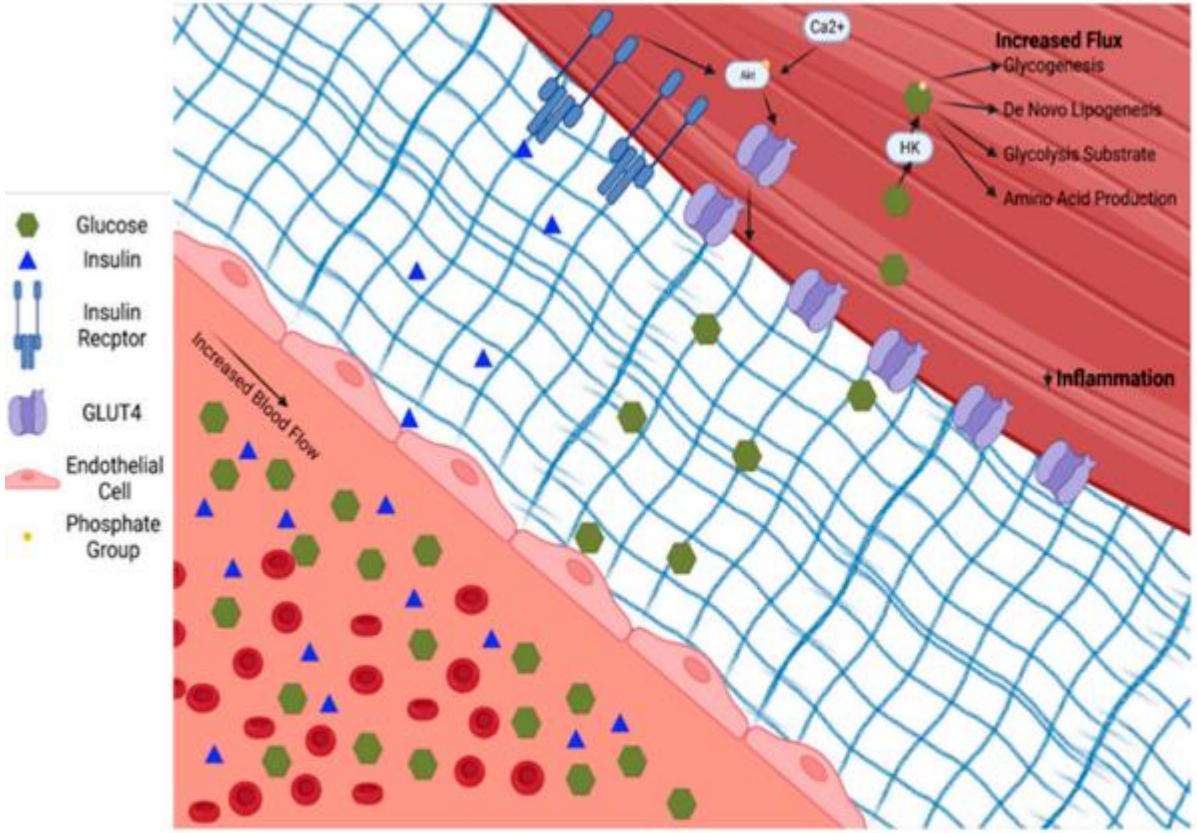
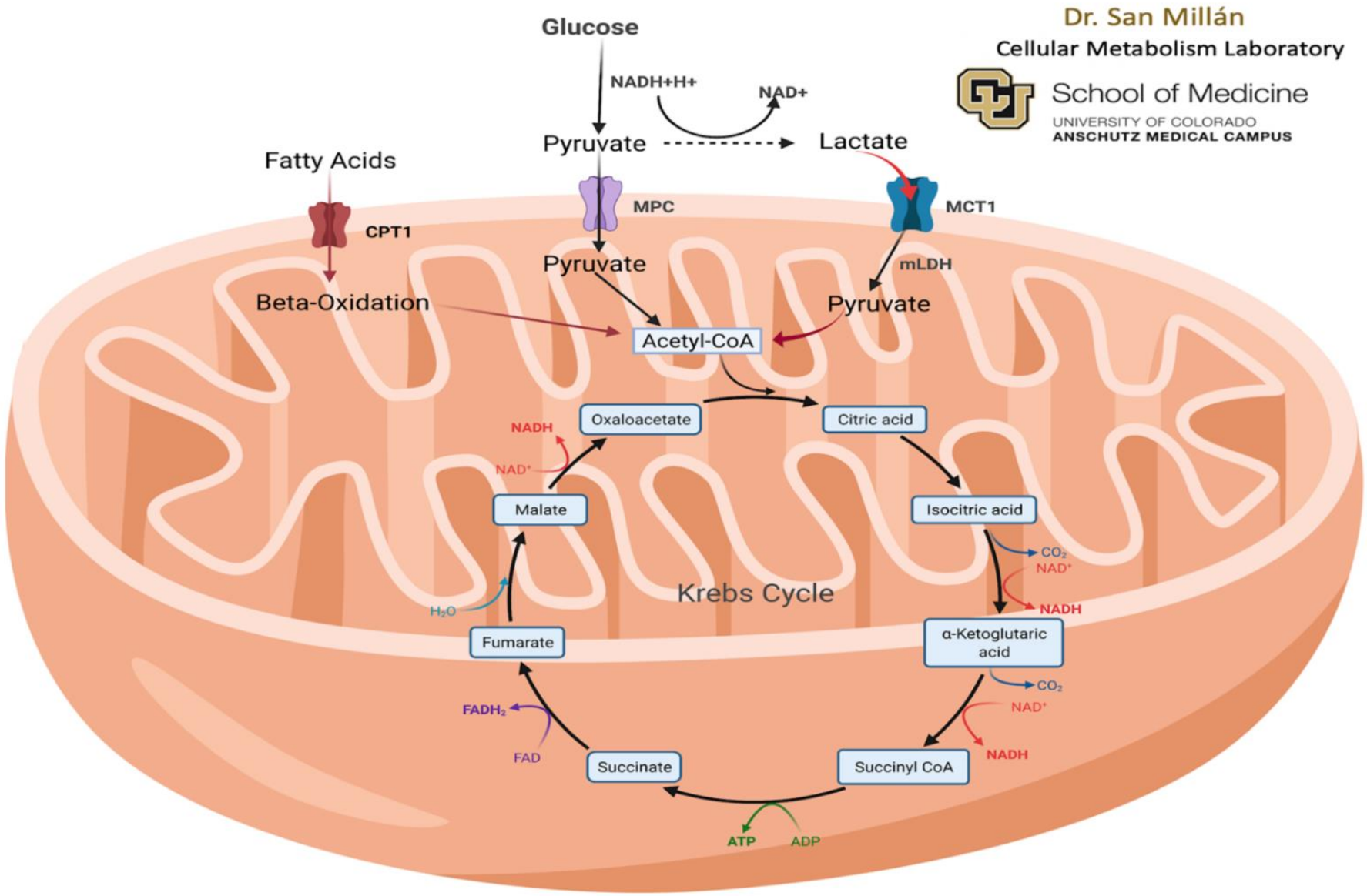


Figure 3. Exercise training restores proper blood flow to skeletal muscle and increases insulin. The extracellular matrix becomes less fibrotic, allowing the passage of glucose and insulin to skeletal muscle. Intramuscular glucose metabolism increased, thereby decreasing the allosteric downregulation of glucose disposal and augmentation of the glucose gradient for facilitated glucose transport. Decreased intracellular DAG and toxic lipid accumulation improves post-receptor insulin action. Hexokinase (HK). Phosphokinase B (Akt).

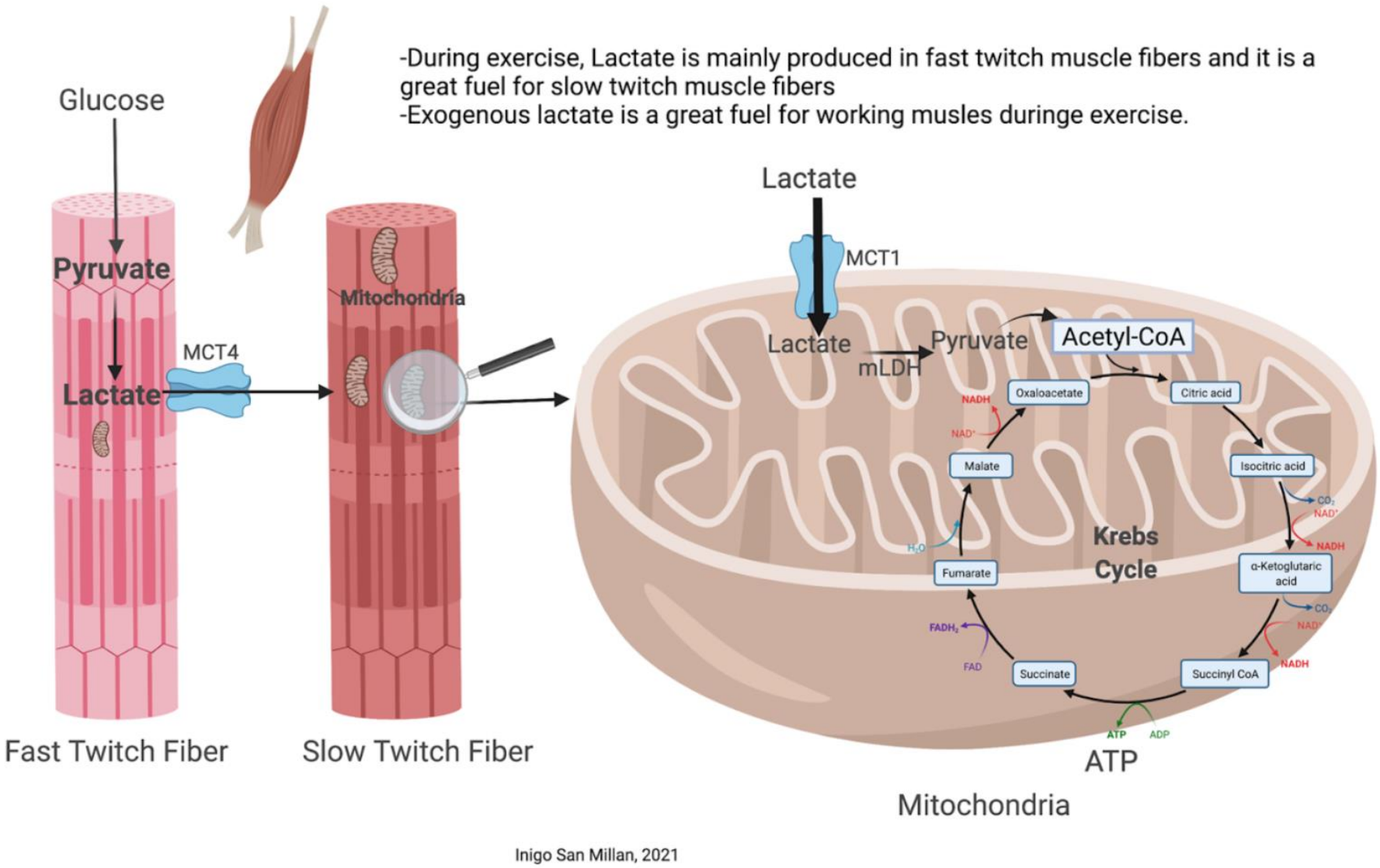
- But there is a **second way** to move those transporters -**muscle contraction!**
- ***Muscle contraction is insulin-independent mechanism of translocating GLUT4 transporters to the cell surface***
- **Incr insulin sensitivity for up to 48 hours after exercise**

Fit athletes require virtually no insulin to translocate glucose into the muscle through the insulin independent pathway

- Insulin brings GLUT4 transporters to the cell surface
- These transporters start bringing glucose inside
- **Fit people with type 1 diabetes should not inject themselves with insulin before exercise**
- Results in **2 signals for translocating these receptors (insulin and muscle contraction), resulting in hypoglycemia**
- Exercise alone is enough to take care of the glucose
- ***This can be applied to people who have insulin resistance (with pre-type 2 diabetes)— exercise right after you eat that carbohydrate***
- This will bring those transporters to the cell surface to move glucose into the cell
- ***You are not going to need insulin!***

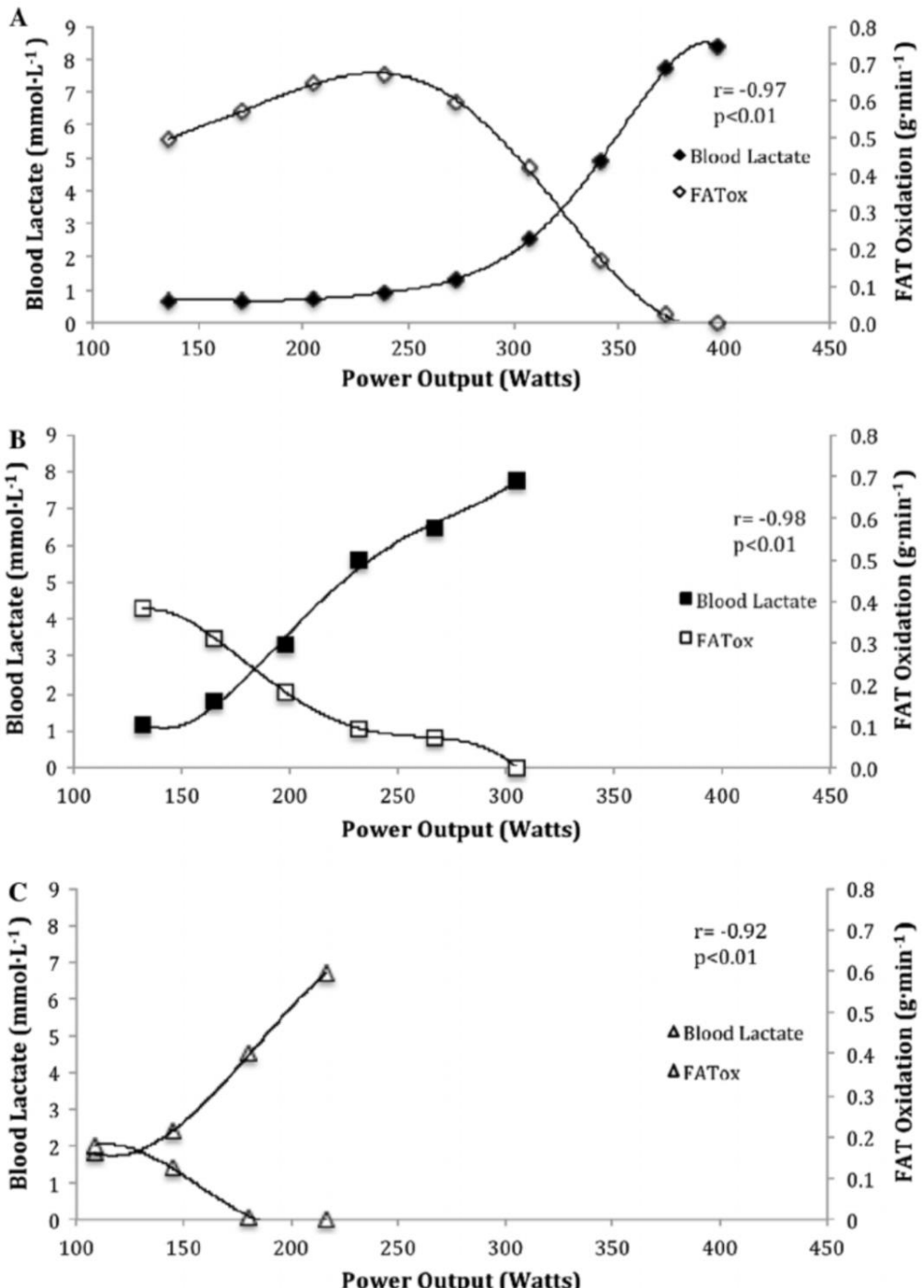


Transporters (MPC, MCT1, and CPT) move metabolites into the mitochondria for oxidation.



Inigo San Millan, 2021

Export of lactate from fast twitch to slow twitch fibers where it can be oxidized



average blood lactate concentrations and FATox (fat oxidation) rates as a function of exercise power

professional endurance athletes

moderately active healthy individuals

individuals with metabolic syndrome. Image credit: (Brooks and Millan, 2018)

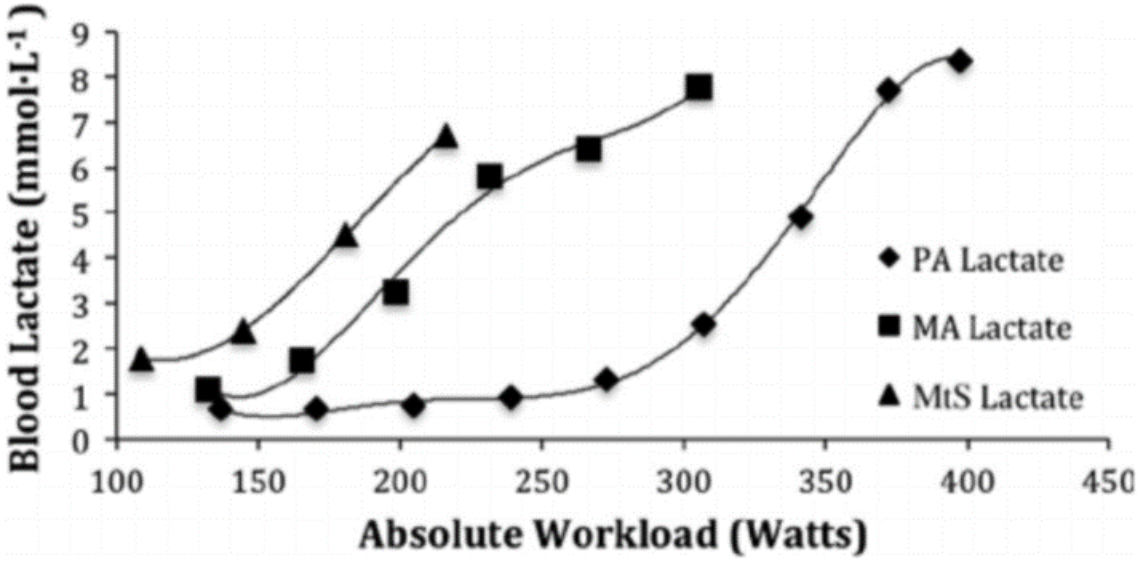


Fig. 1 Relationships between average blood lactate levels and exercise power outputs in international-level PAs, MAs, and individuals with MtS. *PAs* professional endurance athletes, *MAs* moderately active healthy individuals, *MtS* metabolic syndrome

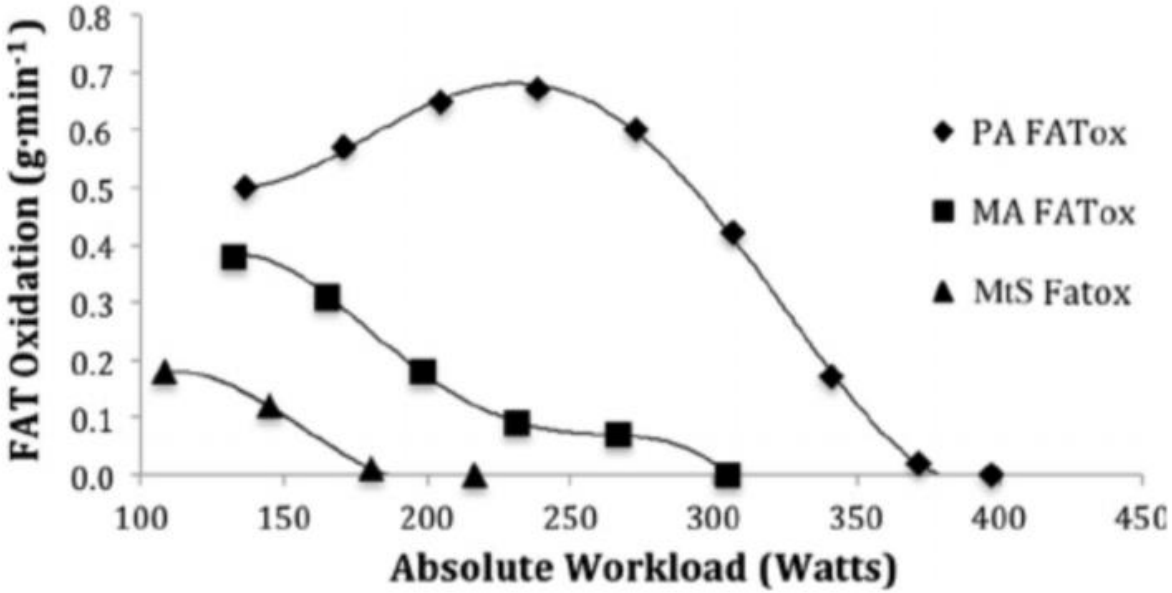


Fig. 2 Relationships between average rates of FATox and exercise power outputs in international-level PAs, MAs, and individuals with MtS. *PAs* professional endurance athletes, *MAs* moderately active healthy individuals, *MtS* metabolic syndrome, *FATox* fat oxidation

RER measuring FATox and corresponding blood lactate at workload in professional athletes (PA), moderately active individuals (MA), and patients with metabolic syndrome (MtS).

Credit: (Brooks and Millan, 2018)

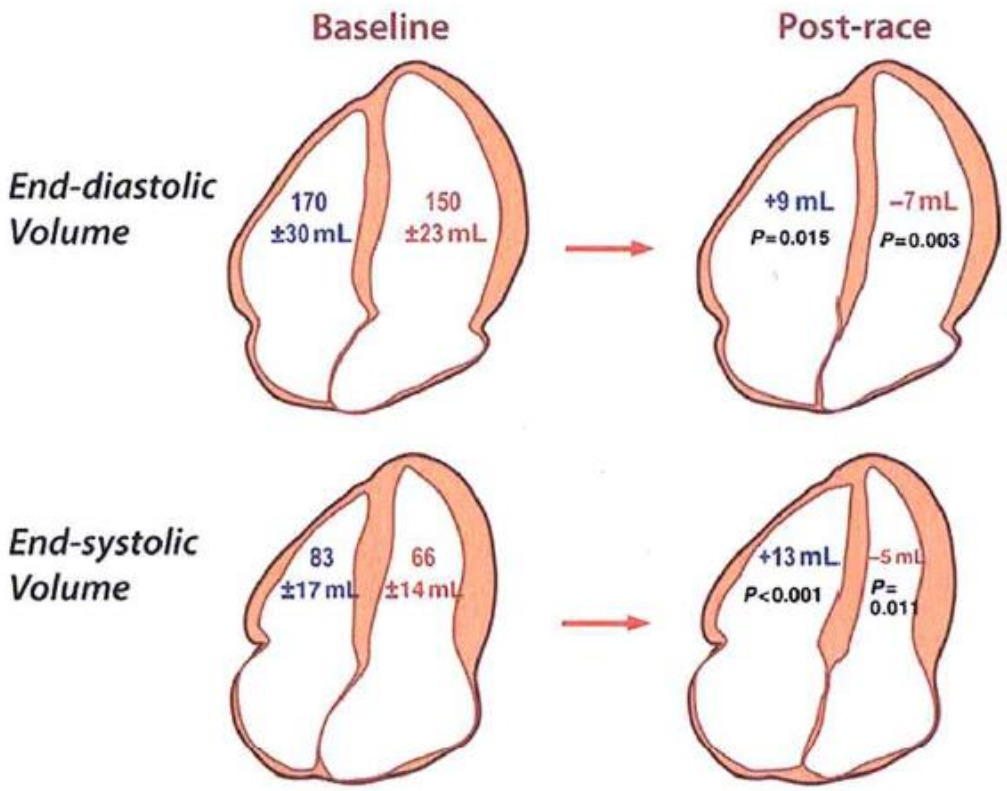
It Can’t Be all Good?

European Heart Journal (2012) 33, 998–1006
doi:10.1093/eurheartj/ehr397

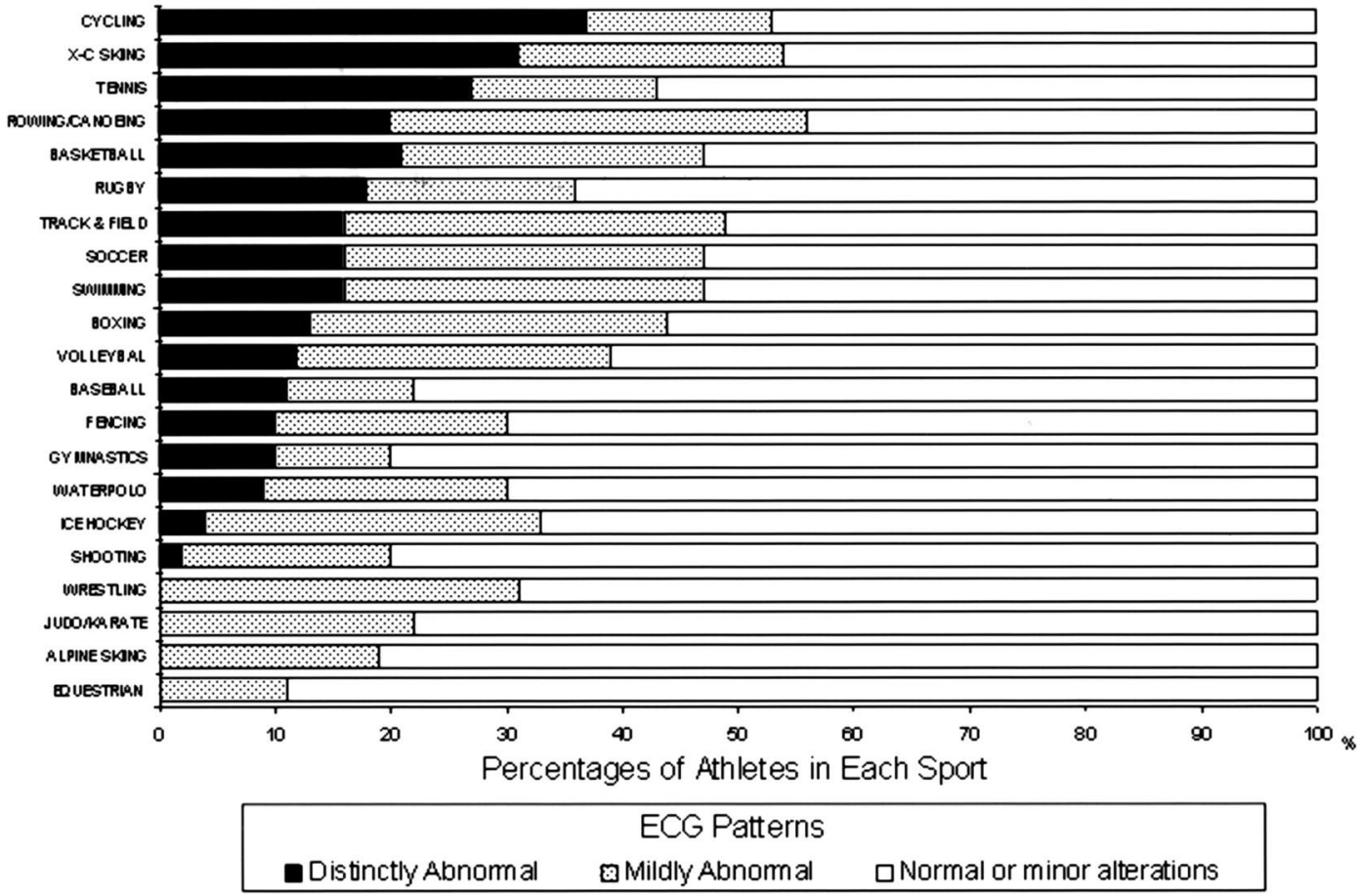
CLINICAL RESEARCH
Exercise

Exercise-induced right ventricular dysfunction and structural remodelling in endurance athletes

André La Gerche[1,2*], Andrew T. Burns[3], Don J. Mooney[3], Warrick J. Inder[1], Andrew J. Taylor[4], Jan Bogaert[5], Andrew I. MacIsaac[3], Hein Heidbüchel[2], and David L. Prior[1,3]

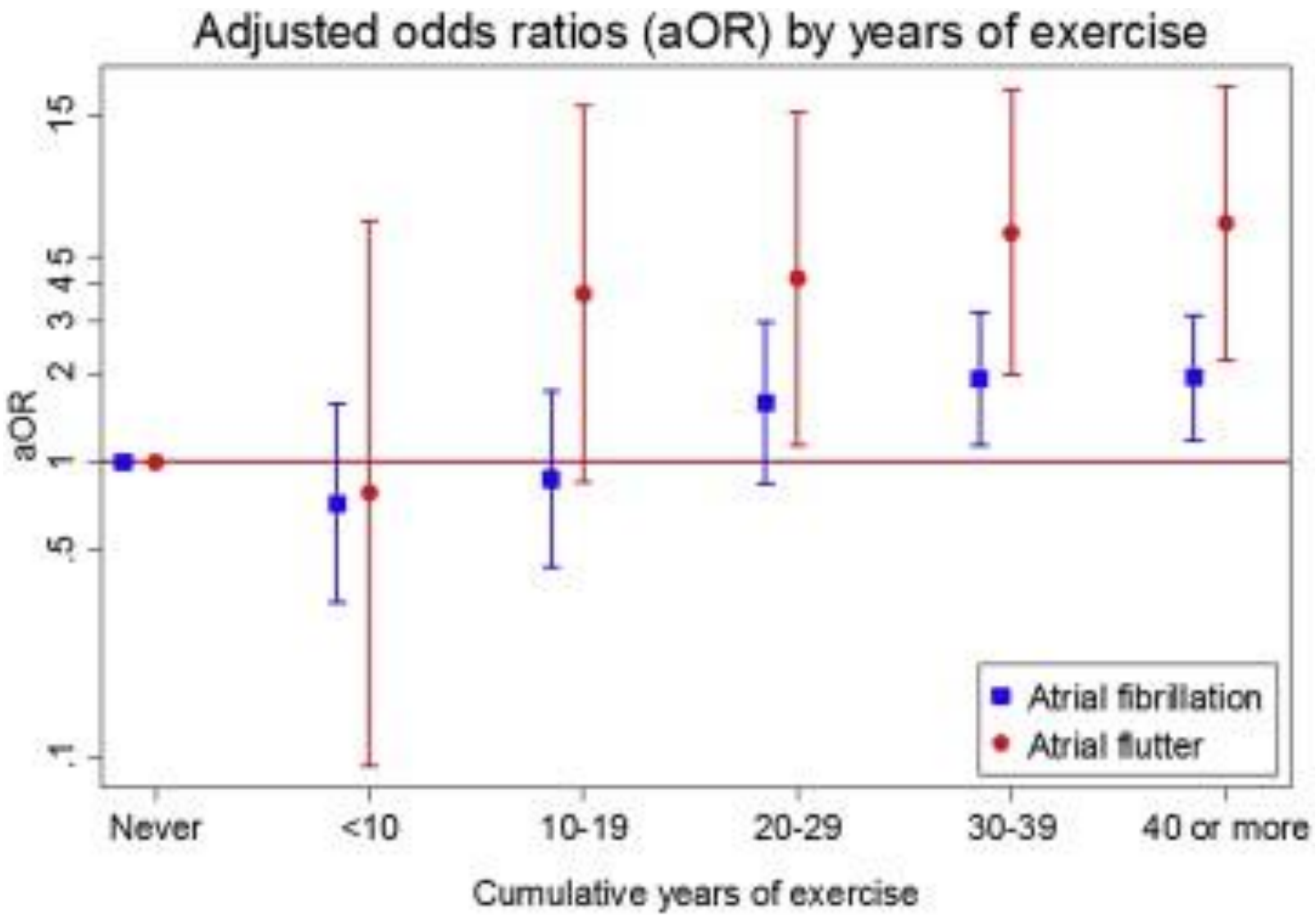


Electrical Remodeling Associated with Different Sports



Maron, B. J. et al. Circulation 2006;114:1633-1644

Effect of Years of Cross Country Skiing on Risk of Atrial Fibrillation and Atrial Flutter



Myrstad American Journal of Cardiology, Volume 114, Issue 8, 2014, 1229 - 1233

Thank you!
Contact
afrundoc@gamil.com

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AMERICAN COLLEGE of CARDIOLOGY

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Sep 05, 2022