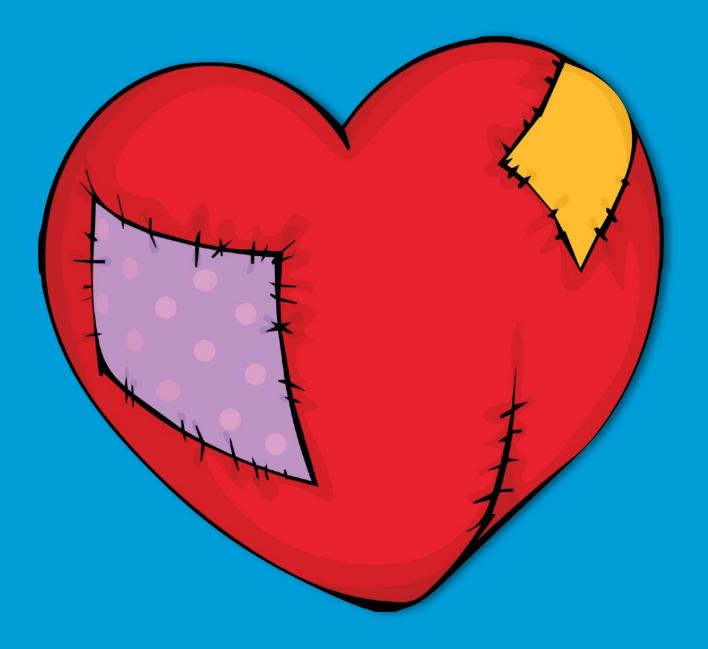
Your Heart Manual



Wojciech Mazur MD and Stephanie Ambach, OMS-1

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About the Author

Dr. Wojciech Mazur

Dr. Mazur is a second-generation cardiologist, and a member of an all-physician family. He earned his medical degree in Poland before he came to the United States where he completed a residency and fellowship at Baylor College of Medicine in Houston, TX.

In 2002, he joined Ohio Heart and Vascular Center, specializing in cardiac imaging (echocardiography, nuclear cardiology, cardiac magnetic resonance, cardiac computed tomography) and clinical cardiology. He serves as Director of Advanced Cardiac Imaging at The Christ Hospital Health Network as well as Professor of Medicine and Pediatrics at The University of Cincinnati and Cincinnati Children's Hospital. He has published more than 170 research articles, books, abstracts and book chapters in the field of cardiology.

Dr. Mazur sees his patients as people, not as a disease or a problem, nor as a task. His focus is not only on how to make the patient well, but also on treating his patient with dignity and respect, while learning their stories and understanding how they tie into their health.

For him, most important aspect of being a physician is to make a lasting difference in his patients' lives.

He strongly believes that the patient is in control of his or her destiny and that changing the way one lives can have a huge impact on their health. In fact, it was recently shown that lifestyle modifications can switch off majority of the genes (143!) causing heart disease and can also lead to regression of blockages! He strongly believes that stress is the main cause of heart disease and focuses on stress management techniques. Common prescriptions in his office include dark chocolate, nuts, laughter, yoga, and adult coloring books. He admits that he has trouble practicing what he preaches, and a top priority of his is to not be judgmental of the patient, even if he or she has trouble with change, because struggle is a part of life!

Dr. Mazur is married with 2 sons and has a dog named Texas. He enjoys, hiking, kayaking, listening to NPR and spending time with family. He is active in local charities: Tender Mercies and Little Sisters of the Poor among others. He truly believes in social justice and is a member of Amnesty International and Sierra Club. Dr. Mazur also believes that access to healthcare is a fundamental right, not a privilege.



Stephanie Ambach is a native to Cincinnati, OH and is currently (2017-2018) a first year Medical Student at Ohio University Heritage College of Osteopathic Medicine in Athens, OH. She completed her undergraduate career at The University of Cincinnati with a Bachelor of Science degree in Health Sciences and a minor in Medical Sciences.

Stephanie began shadowing and working as a Research Assistant to Dr. Mazur in 2014, where she discovered that becoming a Physician was her dream and goal. With Dr. Mazur as a mentor, she learned many aspects of holistic medicine and quickly realized how important it is to look at the patient as full body, mind and soul. As Stephanie continues her career as a Medical Student at OUHCOM she is able to continue to embrace holistic medicine and eager to incorporate this scope of medicine as a medical professional.

In her free time, Stephanie enjoys spending time with her family and dog, Boogie. She also enjoys spending time outdoors camping, hiking and boating.



I would like to thank my beloved wife Eugenia and my sons Andre and Jan for their support and inspiration. A few hundred hours were taken from them, which I can't return
Special thanks to Lisa Ambach, proud mother of co-author Stephanie Ambach for her assistance in creation of this book.

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Preface

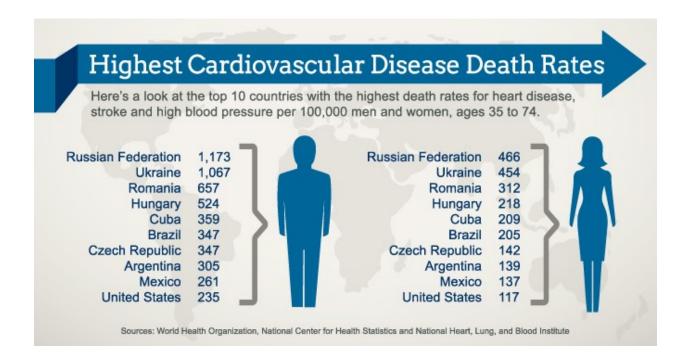
We are pleased to present you with a short book "Your Heart Manual" representing up-to-date summary of over 500 research articles published in peer reviewed medical journals in past decade (most of them in past 2 years!), organized in 21 chapters focusing on the power life style modification and not just medications and procedures. Many recent discoveries contradict previously published recommendations (like that fat is bad for you!). Why? Medical studies are getting bigger (tens to hundreds of thousands of participants) and thus more likely to represent reality. What you will notice reading this book is that all it represents is just plain common sense!

The book contains just facts rather than representing an opinion of a self-proclaimed guru. Adopting healthy life style always includes three elements: be at peace (rather than aiming at being continuously happy, which is not possible!) be active (this includes sex!) and eating well. Heart disease, cancer, stroke, dementia share the same roots and healthy life style can reduce risk of all of them. Yes, thanks to modern medicine we are living longer but this does not always translate into a quality life. Changing life style, regardless of your age or your health will result not only on longer but happier existence! It is of outmost importance to understand that chronic stress, depression, anger and other negative emotions can cancel benefits of diet and exercise. Becoming mindful, free from negative emotions is the first and most important (and challenging) part of the change! There is no 1-800 toll free number to call to order a magic pill, everything you really need is in your local grocery store and in your mind.

Enjoy the journey!

Wojciech Mazur, MD

Stephanie Ambach, Medical Student



Health data compiled in 2015 report from over 190 countries demonstrated that heart disease remains the No. 1 global cause of death with 17.3 million deaths each year, with expected to rise to more than 23.6 million by 2030.

Stroke remains the No. 2 cause of death worldwide. The stroke death rate the number of deaths per 100,000 people decreased between 1990 and 2010. However, the number of people having first and recurrent strokes each year went up, reaching 33 million in 2010.

11.4 million worldwide deaths among 30- to 69-year-olds and 15.9 million deaths among people 70 and older could be delayed or prevented in 2025 if global targets are met for reducing tobacco and alcohol use, decreasing salt consumption, managing obesity and lowering blood pressure and blood sugar levels.

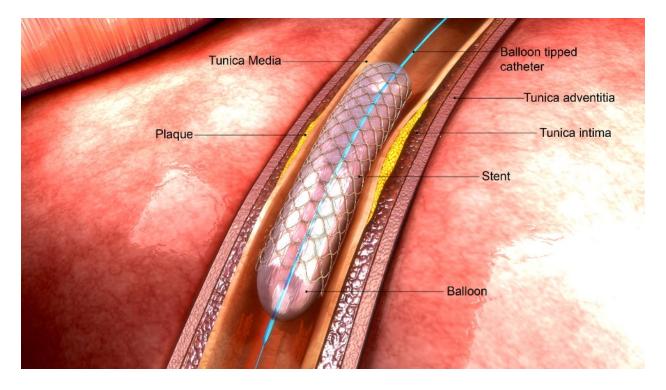
Fewer Americans have been dying from heart disease and stroke since the 1980s, and the new report found cardiovascular disease deaths in the U.S. continued to drop from 2001 to 2011, by 30.8 percent. Much of the progress comes from better use of medical therapies in patients with a history of heart disease and stroke and from lifestyle changes that are curbing the risk.

Other relevant facts:

- Heart disease remains the nation's leading cause of death in the U.S., a ranking it has held since 1921. Stroke still ranks fourth.
- An estimated 85.6 million people in the U.S. are living with cardiovascular diseases, including heart attack, stroke, high blood pressure and chest pain.
- Among U.S. adults, 32.6 percent, about 80 million have high blood pressure.
- Despite an overall 30.8 percent drop in cardiovascular disease death rates from 2001 to 2011, the high blood pressure death rate increased 13.2 percent over that same time. [1]

In a recent study (INTERHEART surveying 47,269 individuals) researchers examined data for eight modifiable risk factors: less than 4 hours a week of moderate exercise; obesity (BMI >30 kg/m², a surrogate for abdominal obesity); eating less than five fruits and vegetables a day; smoking within the past 12 months; high stress; more than four alcoholic drinks/week, type 2 diabetes; and hypertension and discovered that one in five individuals who had the highest risk of having a cardiovascular event (since they had five or more modifiable risk factors did not think that they needed to improve their health habits. Close to three-quarters of the survey respondents (74%) reported that they needed to change some health behaviors, and 81 percent planned to do so in the coming year. Of those who saw a need to make lifestyle changes, 56 percent reported that they would be hindered, most notably by a lack of willpower, followed by a busy work schedule and family responsibilities. Sound familiar? [2]

Remember: stent in the artery may have saved your life and relieved angina but it did not cure the disease that resulted in plaque buildup in the first place!



Is heart disease unavoidable? Answer: no

- The Tsimane are a native population of hunters and gatherers in the Bolivian Amazon The group has preserved their culture and language for thousands of years. Their way of life is incredibly good at protecting the heart!
- Of Tsimane people over age 40, about 85 percent have no atherosclerosis (plaque buildup in their hearts) and nearly two-thirds over age 75 were free of coronary artery plaque.
- Comparing that to American population, the statistics were just the opposite: nearly 85 percent of Americans over age 45 have atherosclerosis with only 14 percent are free of the plaque.
- That data means the heart of an 80-year-old Tsimane has the "vascular age" of an American in his or her mid-50s. The Tsimane have the lowest levels of coronary artery disease ever recorded in the world!

What is their secret?

- To establish prevalence of heart disease, researchers measured the amount of calcium deposited in the coronary arteries of more than 700 Tsimanes between age 40 and 94 using simple CT scan of the heart to measure coronary calcium (calcified plaque in the heart) as well as blood pressure, body-mass index, cholesterol levels and inflammation levels.
- The group had low blood pressure and low cholesterol, on average, But they have low levels of the "good" cholesterol and high levels of chronic inflammation, which has been linked to heart disease in Western populations.
- What about weight? None of the Tsimane are obese but about a quarter of adults qualify as "overweight." The average BMI (body mass index) was about 24, which is near the upper end of normal, (with a BMI of ≥25 considered overweight). No super lean individuals!
- The Tsimane get lots of exercise, but none of it was intense exercise. Tsimanes walk about 7 1/2 miles each day and were active for more than 90 percent of their wake time. Americans, in contrast spend about half their waking hours sitting down.

Tsimane Diet (not meat packed paleo diet!)

• More than 70 percent of their calories come from complex carbohydrates packed with fiber, such as corn, cassava and plantains. The remaining 30 percent of the calories are split evenly between animal protein and fat (fish, bush meat). The Tsimane eat no transfat and very little simple (refined) sugars. In contrast, Americans still eat more than a gram of transfat and 22 teaspoons of extra sugar per day! [3]



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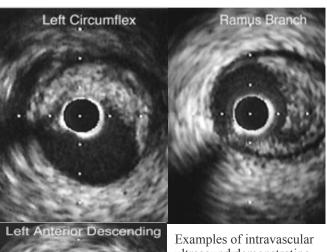
What about my genetic burden and my extensive family history of heart disease in early age?

Answer: Your genes are not your destiny! They can be switched on and off depending on your behavior!

A 2014 study looked at the effects of lifestyle changes on the expression of genes that are associated with cardiovascular disease. The study included 63 control participants and 63 participants who abided to decreased fat intake and increased physical activity.

- For 52 weeks these participants ate a very low-fat vegetarian diet, completed moderate aerobic exercise 180 minutes per week, and completed 1 hour of stress management a day and went to weekly support sessions.
- The diet participants abided by emphasized whole grains, fruits, vegetables, legumes, and soy products and their exercise regimen such as walking, rowing and water aerobics. Their stress management included yoga, meditation, relaxation, imagery and deep breathing.
- By the end of the 52 weeks 143 genes responsible for plaque buildup were differently expressed: either down regulated (less active) or switched off compared to baseline. Control group participants showed little change in gene expression.

- Prescription medications did not alter gene expression.[4]
- In a large 2016 study involving 55,685 participants, genetic and lifestyle factors were independently associated with susceptibility to coronary artery disease. The relative risk of incident coronary events (heart attacks, deaths etc.) was 91 percent higher among participants at high genetic risk.
- Among participants at high genetic risk, a favorable lifestyle (defined as no current smoking, no obesity, regular physical activity, and a healthy diet) was associated with a nearly 50 percent lower relative risk of coronary artery disease than was an unfavorable lifestyle![5]
- Translation: if you have family history of early heart disease, you will need to put extra work on your life style to avoid the faith of your ancestors!



Left Anterior Descending

Examples of intravascular ultrasound demonstrating plaque in different coronary arteries of teenagers.

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socio economic class was determined. 20 out of 52 have evidence of atherosclerosis in different vessels (aorta, heart, brain). The 20 mummies with atherosclerosis were older at time of death (mean age 45 years) than mummies without no atherosclerosis (mean age 34 years). Two mummies had evidence of severe arterial atherosclerosis with calcifications in virtually every arterial bed)

Is atherosclerosis affecting older people only?

No. In a 2001 study, of teenagers and young adults (< 20 year old) who died from accidental deaths and become heart transplant donors, researchers discovered using intravascular ultrasound (performed within 1 month after heart transplant) that 17 percent (1 in 6) have evidence of atherosclerosis! [6]

Is atherosclerosis a modern disease? Answer: No

In a 2011 study, group of Egyptian cardiologist, performed CT scan on 52 ancient mummies. The mummies lived between 1981 BCE and 364 CE. Mean estimated age at death was 38.1 ± 12.0 years. Based on historical records and expensive mummification techniques involved, high



Ancient Egyptian mummy being examined inside an CT scanner.

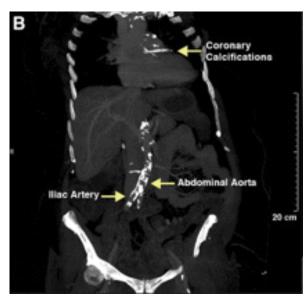
Why???

• Tobacco was unavailable at those times. Hieroglyphic inscriptions on Egyptian temple walls indicate that beef, sheep, goats, wildfowl, bread, and cake were regularly consumed suggested that the ancient Egyptian diet consumed by royalty and social elites may have been atherogenic, (particularly among the clergy who consumed the ritual feasts left by families mourning their deceased relatives). It is possible, that due to their high status, they were carried by their servants rather than walking. Moral of this story: Nature really does not care about your income and social position. Nature is simply a great equalizer! [7]

Can coronary artery disease (plaque buildup) be reversed without statins?

Yes! It does however take some hard work! And we have known about it since 1990!

- In a landmark study Dean Ornish demonstrated that Intensive lifestyle changes (10% fat whole foods vegetarian diet, aerobic exercise, stress management training, smoking cessation, group psychosocial support) can regress heart disease.
- After 1 year, investigators found that experimental group participants were able to make and maintain intensive lifestyle changes and had a 37.2 percent reduction in lowdensity lipoprotein (LDL) cholesterol levels and a 91 percent reduction in the frequency of anginal episodes.



Example of extensive vascular calcification seen in a Egyptian mummy.

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- Average percent diameter stenosis regressed from 40.0 percent at baseline to 37.8 percent 1 year later, a change that was correlated with the degree of lifestyle change.
- In contrast, patients in the usual-care control group made more moderate changes in lifestyle, reduced LDL cholesterol levels by 6 percent, and had a 165 percent increase in the frequency of reported anginal episodes. Average percent diameter stenosis progressed from 42.7 percent to 46.1 percent. [8]
- At 5 years there was additional regression of stenosis: In the experimental group, the average percent diameter stenosis decreased by 3.1 absolute percentage points after 5 years (a 7.9% relative improvement).
- In contrast, the average percent diameter stenosis in the control group by11.8 percentage points after 5 years (a 27.7% relative worsening). [9]

I don't have heart disease; how do I know that I am at risk of future heart attack?

These are some steps that you can take:

- 1. Calculate your 10-year risk of heart disease using Framingham Risk Calculator. (https://www.cvdriskchecksecure.com/framinghamriskscore.aspx)
- 2. Ask your doctor to order coronary artery calcium (CAC) a quick CT scan of your heart to figure your vascular age (the same test used in Tsimane and Egyptian mummy's research).

What does calcium score mean?

This depends on mainly on your age and lesser extent on sex and race. Results are plugged into MESA calcium score calculator (https://www.mesa-nhlbi.org/calcium/input.aspx), which calculates which percentile you are for your age, sex and race.

For example:

If you are 45-year-old female with calcium score of 20, you are at 97th percentile for your group: out of hundred only 3 individuals will have more plaque in their heart than you! You are in trouble if you don't take care of yourself! But if you are 80-year-old female with calcium score of 20, you are in the 25th percentile for your group! Almost a Tsimane!

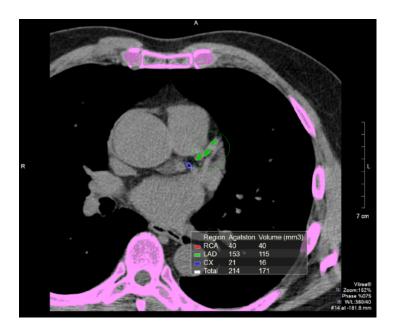
My calcium score was zero, what does it mean?

It means great news: your heart just got a 15 year warranty period!!!! (Defined as <1% annual mortality rate) especially if you are in the low to intermediate risk by Framingham Risk Calculator [10]

My calcium score was 55, 3 years ago; I completely changed my life style and taking all prescribed medications including statin and aspirin. My calcium score jumped to over 300! Why is this happening?

Non-contrast CT scan detects only calcified plaques, which are just the "tip of an iceberg", most of the plaques in the coronary vessels are "soft" without calcium. Soft plaque is most dangerous as it may rupture, leading to vessel thrombosis (a clot forming on top of a plaque leading to cessation of blood and heart attack). Calcific plaque is considered stable, not leading to heart attacks. Healing of soft plaque occurs through calcification as such increase in calcium score may just reflect that your coronary artery disease is stabilizing and healing. This was mostly observed in patients taking high dose statin (another mechanism other than shrinking the plaque that statins convert unstable, at high risk of rupture plaques into stable ones). [11]

But if your calcium score is climbing, while not taking medications and not taking care of yourself: Beware the end is near!!!!



Example of calcium score CT scan: green depicts calcified plaque in a coronary vessel LAD (left anterior descending artery) This test established amount of calcified plaque in the coronary vessels but does not provide information if the plaque interferes with blood flow or not.

Where people are living longer and healthier: The Blue Zones

The Blue Zones concept came from a demographic work done by Gianni Pes and Michel Poulain concerning the longevity of the people born between 1800 and 1900 in Sardinia, Italy. Doing so, they drew blue circles around the areas with the highest concentration of centenarians, referring to them as Blue Zones.

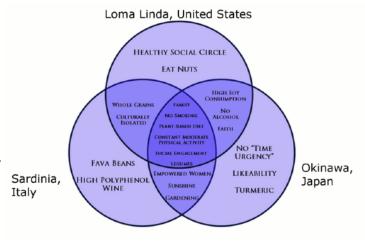
In 2004, Dan Buettner, an American explorer and educator, joined National Geographic and a team of world-class longevity researchers to carry out a project to research locations around the world and identify the spot where people are living healthier for the longest periods. Buettner and his team discovered that in each of these areas, the rate of centenarians was 10 times greater than that in the US, as reported in the Bluezones.com By studying the correlation between local lifestyles and longevity, they found that all the Blue Zone residents share the same nine characteristics for living healthier longer:



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Characteristics of Blue Zone Residents

- 1. They move naturally finding ways to move more rather than using vehicular transport
- 2. Waking up with a purpose they know what their purpose is each day
- 3. Lessened stress they work out a variety of routines to de-stress or avoid it altogether
- 4. 80 percent Rule they stop eating when their stomach is 80 percent full, rather than 100 percent (or more!) Legume and bean-based diets, modest meat consumption



- 5. Drink alcohol moderately and regularly (effect of alcohol however is still disputed by some, see chapter 2)
- 6. They find a place to belong all but five of the 263 centenarians interviewed belonged to some faith-based community
- 7. Family first before all other concerns, they value family
- 8. They source the right tribe attend social circles that supported healthy behaviors

Ikaria: where people forget to die...

Ikaria is a small village of 300 residents on the Greek island of Ikaria, a nine-hour ferry ride across the Aegean Sea from Athens with one major unique feature: one third of the island's population lives to be more than 90 years old! Ikarians make an effort to stay closely connected to their families and neighbors, and the elderly play significant roles in the community. Grandparents often help raise grandchildren or run businesses. A 102-year-old women credits her longevity to her outlook on life. "Do not want more than what you really need. If you envy others, that can only give you stress," Business owners open and close their doors on no set schedule. Shops operate on an honor system: customers take what they please and leave money on the counter in return. Levels of stress are very low, no one makes appointments, even to see a doctor! (would not work in my office however...) What's there not to like?

Life in Ikaria











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Do I have to do everything in this book to get the benefits?

No, but the more you do the bigger the gain!

Resources for Information on Cardiac Health:

- American Heart Association: www.heart.org
- mylifecheck.heart.org, a website (provided by AHA) where people learn how to improve their health by following "Life's Simple 7": get active, control cholesterol, eat better, manage blood pressure, lose weight, reduce blood sugar and quit smoking.
- http://www.health.harvard.edu/ Great website from Harvard Medical School with frequent updates on life style modification and your health.
- Medscape.com: free website (registration required) updated daily on most recent relevant cardiovascular discoveries, with excellent search engine for specific topics.
- Media Health sections of NPR.org, BBC.com and NYT.com: solid reporting on interesting medical information, translating articles into less medical, more understandable language.

References:

- 1. Mozaffarian, D., et al., Heart disease and stroke statistics--2015 update: a report from the American Heart Association. Circulation, 2015. **131**(4): p. e29-322.
- 2. Ramirez, F.D., et al., Association Between Self-Reported PotentiallyModifiable Cardiac Risk Factors and Perceived Need to Improve Physical Health: A Population-Based Study. 2017.
- 3. Kaplan, H., Thompson Randall, Trumble, Benjamin, et al.. Coronary atherosclerosis in indigenous South American Tsimane: a cross-sectional cohort study The Lancet. The Lancet, 2017. **389**(10080): p. 1730-1739.
- 4. Ellsworth, D.L., et al., Intensive Cardiovascular Risk Reduction Induces Sustainable Changes in Expression of Genes and Pathways Important to Vascular Function. Circulation: Cardiovascular Genetics, 2014. **7**(2): p. 151-60.
- 5. Khera, A.V., et al., Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. http://dx.doi.org/10.1056/NEJMoa1605086, 2016.
- 6. Tuzcu, E.M., et al., High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: evidence from intravascular ultrasound. Circulation, 2001. **103**(22): p. 2705-10.
- 7. Allam, A., Thompson, Randall, Wann, Samuel, Minamoto, Michael et al., Atherosclerosis in Ancient Egyptian Mummies: The Horus Study ScienceDirect. JACC:Cardiovascular Imagining, 2011. **4**(4): p. 315-327.
- 8. Ornish, D., et al., Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. Lancet, 1990. **336**(8708): p. 129-33.
- 9. Ornish, D., et al., Intensive Lifestyle Changes for Reversal of Coronary Heart Disease. JAMA, 1998. **280**(23): p. 2001-2007.
- 10. Valenti, V., et al., A 15-Year Warranty Period for Asymptomatic Individuals Without Coronary Artery Calcium: A Prospective Follow-Up of 9,715 Individuals. JACC Cardiovasc Imaging, 2015. **8**(8): p. 900-9.
- 11. Puri, R., et al., Impact of statins on serial coronary calcification during atheroma progression and regression. J Am Coll Cardiol, 2015. **65**(13): p. 1273-82.

The Evolution of the Human Diet

The human diet began with early primates' diet included plants insects and larva. About two million years ago meat was incorporated into diet. Meat became a large aspect of hunters and gathers diet as it made up half of their calories. It is believed that the extra energy coming from meat aided in the development of advanced hominid brain. Bulbs and tubers were also added to the diet about one to two million years ago and were a large part of hunter and gatherers diets when meat was limited

A major turning point in the human diet was when agriculture was developed six to ten thousand years ago. This included grains, dairy and legumes. Agriculture resulted in a population growth as it created a plentiful and predictable food supply for traditional non-hunters. This population growth did not mean a healthier population. The new diet also brought cavities, parasites, infectious diseases and developmental delays.

In the last 100 years grain processing removed germination center of the kernel, the most nutritional part, more processed food was introduced and trans-fats and refined carbohydrates such as high fructose corn syrup were introduced. Fructose causes our bodies to store fat. When we consume fructose, we activate an enzyme, fructokinase, which causes our body cells to store fat. [1]

The first sugar was recorded in England in 1100. Its price in London in 1300 was equal to US \$100 per kilo at today's price. Sugar intake started low in 1700's with the average person consuming 4 lbs per year increasing to 18 lbs in 1800's and 90 lbs 1900's.

Today about 50 percent of Americans consume 180 lbs. of sugar per year. [2] High fructose corn syrup was introduced to food industry in the late 1960s.

Thrifty Gene Hypothesis

Societies in the past struggled through phases of feasting and famine. During this time, the human body evolved to select "thrifty genes" that allowed for very efficient fat storage and energy utilization. Humans, who were better at storing and utilizing food during the time of feasting, were more likely to survive the famine. (natural selection) Now, we are exposed to excessive amount of often unhealthy and processed foods along with "thrifty genes" allowing us to rapidly convert it into fat (storage) but we no longer utilize stored energy during time of famine, leading to weight gain and eventually obesity. [3]



Unhealthy (but tasty!) Food

The Western Diet

- High consumption of red meat, sugar, high-fat foods and dairy products, eggs and refined grains.
- Compared to a prudent diet, which has higher levels of fruits, vegetables, wholegrain foods, poultry and fish, the Western diet, increases the risk of heart attack by 92 percent. In other words, the Western diet increases your risk for a heart attack, while a prudent diet (such as Mediterranean) lowers it. [4]

The Southern Diet

- A diet rich in fried foods, processed meat and sweetened beverages.
- Diet most prevalent in Delaware, Louisiana, Mississippi, Alabama, Georgia, Missouri, Arkansas, Michigan and Maryland.
- Individuals who eat a southern diet have a 56 percent higher risk of heart disease, 50 percent increase in risk of death for individuals with kidney disease, and a 30 percent higher risk of stroke. [5]
- Occasional junk food is ok! More studies support the fact that is not necessarily that junk food causes heart disease but rather lack of healthy food does! [6]





Killer Fried potatoes...

In a longitudinal analysis (which included 4440 participants aged 45–79 at baseline with an 8-y follow-up) researchers investigated effect of potatoes consumption on risk of death. During the 8-y follow-up, 236 participants died. After adjustment for 14 potential baseline confounders (different risk factors for death) consuming fried potatoes 2-3 x a week increased risk of death by 95 percent and over 3x a week: 126 percent! Non-fried potatoes had no effect on mortality. [7]



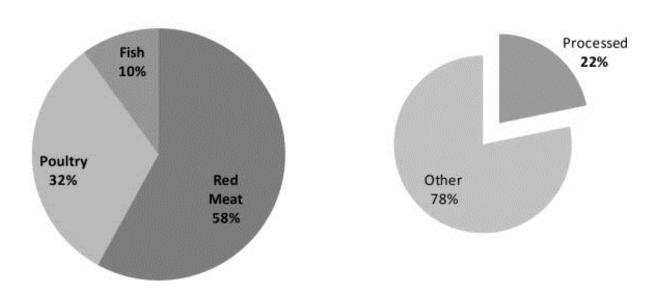
Red Meat and Processed Meats

Brief History of Red Meat Consumption

All countries eat more meat when their incomes grow and they have the economic wherewithal to eat more meat: seems to be preferences built into us. Americans eat meat (3 times more than average for the rest of the planet) because they can afford it and they eat more than other rich countries. Meat is relatively cheap in the U.S., compared to Japan or many countries in Europe. Almost two centuries ago, meat was one reason why immigrants found America so amazing. When the Irish came in the 1840s, they wrote letters back saying, "I eat meat every day" And they got letters back saying, "You must be kidding. It can't be true." American appetite for beef

hit a peak in 1976, and has been plummeting ever since. It's now down by one-third. Instead, the average American is eating twice as much chicken (mainly because of plummeting chicken price) Source, NPR 2012 The Making Of Meat-Eating America Despite a shift toward higher poultry consumption; red meat still represents the largest proportion of meat consumed in the U.S (58 percent).





Twenty-two percent of the meat consumed in the U.S. is processed. Average meat consumption is 128 g (4.5 oz). [8]

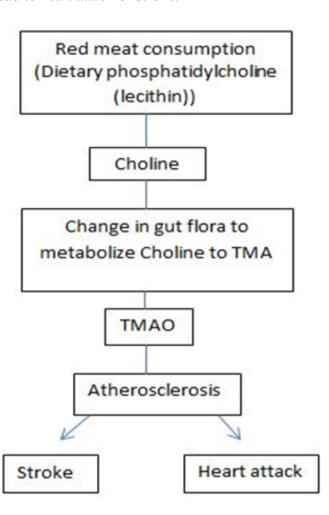
Issues with red meat

Never in history of humanity did human consume so much meat! Using very sophisticated tools recent study concluded the first farmers, who lived around 12,000 years ago, likely ate no more than 40 to 50 percent of their protein from animal sources. Those people ate a diet more similar to subsistence farmers in modern-day India or China. Hunter-gatherers from the Paleolithic period also ate less meat. It appears that they consumed very balanced diet! It was likely result of pure practicality: the owner of red meat was mean and strong; fatalities were common during hunt, much less so with fish and chicken.... [9]

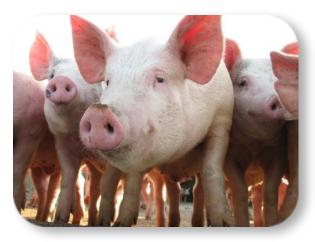
It gets much worse with processing....

- Processed red meats contain sodium, nitrates and phosphates that contribute to increased risk of heart failure.
- A study concluded that for every two slices of ham you consume daily, your risk of dying from a heart related event increases by 38 percent! [10]

- Eating the equivalent of one hot dog per day is associated with a 42 percent higher risk of heart disease and 19 percent increased risk of diabetes.
- Processed meats have more adverse effects on the heart than unprocessed red meat, as they contain four times the sodium and 50 percent more preservatives. [11]
- When red meat is consumed you are also consuming dietary phosphatidylcholine (lecithin), which is a major source of choline. This choline reaches the gut and serves as fuel for the bacteria in the gut (gut flora) to metabolize the choline nutrients into trimethylamine and further into trimethylamine-N-oxide (TMAO). TMAO is known to cause an increase in cholesterol and atherosclerosis which can lead to heart attack or stroke.
- A new test has been developed which measures the level of TMAO in the blood. Higher levels of TMAO in the blood have been linked to a higher risk of heart attack, stroke and death.
- People with higher levels of TMAO amounts are 2.5 times more susceptible to experience heart attack and death. [12]
- Baby aspirin lowers blood TMAO levels



Pork: Not Another White Meat!





The more red meat you eat, the greater your risk of dying from one of eight diseases.

- Researchers studied more than 536,000 men and women ages 50 to 71, tracking their diet and health for an average of 16 years. They recorded consumption of total meat, processed and unprocessed red meat (beef, lamb and pork), and white meat (poultry and fish).
- Compared with the one-fifth of people who ate the least red meat, the one-fifth who ate the most had a 26 percent increased risk of death from various causes? High red meat consumption increased the rate of dying from cancer, heart disease, respiratory disease, stroke, diabetes, infections, kidney disease and liver disease.
- White meat (in this study: fish and poultry), was beneficial. The researchers found that those who ate the highest proportion of white meat had a 25 percent reduced risk of dying from various causes compared with those who ate the least white meat. [13]

How the Sugar Industry Changed Our Diet...

In 1967, "Effects of fats, carbohydrates on atherosclerotic disease," an article in the New England Journal of medicine came out highlighting the minimal effects of sugar. This article lead to a change in dietary guidelines that focused on low or nonfat diets and the use of high fructose corn syrup. Only in 2016, it was disclosed that the original article was funded by the Sugar Research Foundation and physicians authoring the study received close to \$50,000 in current dollar value. This was a clear ethical violation by current standards. This change triggered the epidemics of heart disease, obesity and diabetes.

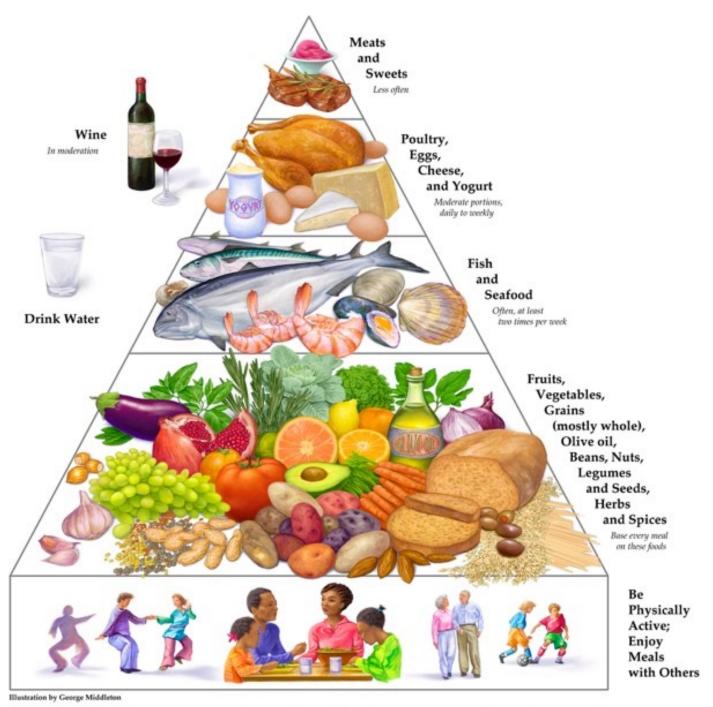
• Fructose intake can have an increased affect on an individual's central appetite control by increasing ghrelin ("hunger hormone") blood levels. Fructose also decreases activation of brain satiety (the state of felling full). This makes you want to eat more!

- Fructose can also affect our cognitive function by impairing learning and memory, reduce neurogenesis (growth of new brain cells) and increases brain insulin resistance. [14]
- Added sugars contribute to high blood pressure, high cholesterol and obesity.
- Common foods that contain added sugars include soft drinks, candy, cakes, cookies, fruit drinks and sweetened yogurts.
- Consumption of one or two sugar sweetened drinks per day is associated with a 26 percent greater risk of developing type 2 diabetes and 20 percent increased risk of developing metabolic syndrome (obesity, hypertension, abnormal cholesterol and diabetes). [15]
- A 2014 study with 9000 participants showed that those who get 17 to 21 percent of their calories from added sugars have a 38 percent higher risk of dying from heart disease. [16]
- Individuals who consume more that 25 percent or more of their daily calories from added sugar are two times more likely to die from heart disease compared to those who eat less than 10 percent of their calories from added sugar. [16]
- The average adult consumes about 22 teaspoons of sugar daily, while the recommended amount is no more than 6 teaspoons a day for woman and no more than 9 for men. [17]
- A 12 ounce can of soda contains about 9 teaspoons of sugar. This one can of soda puts woman over the recommended amount of daily sugar for a day and men at the recommended value.



Mediterranean Diet Pyramid

A contemporary approach to delicious, healthy eating



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Diet Soda

- Another large study that followed thousands of residents of San Antonio for 10 years found those who drank more than 21 servings of diet drinks a week were at twice the risk of becoming overweight or obese, and the more diet soda people drank, the greater the risk.
- Pregnant women consuming 1 diet drink per day, doubles the risk that their infant will be overweight by age 1. [18]
- When you consume sugar the taste buds send signals to the brain's primary taste cortex. Neurons then send projections to the brain's primary reward pathway and dopamine is released. Less dopamine is released with each bite of food so eventually you get full and stop eating.

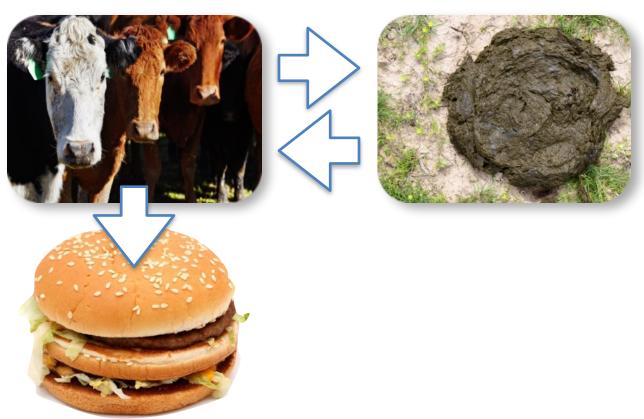


- Artificial sweeteners trick the brain and although the primary taste pathway is activated, only
 real sugar is able to activate a significant response in the reward pathway. Artificial sweeteners
 cause a lack of complete satisfaction which leads to increased appetite and eventually to
 weight gain.
- A large 2017 study (pooled results from seven randomized controlled trials with 1003 participants (median follow-up 6 months) and 30 cohort studies with 405,907 participants (median follow-up 10 years) evaluated effects of artificial sweeteners. In participants who were obese or overweight, two longer trials showed significant weight loss with artificial sweeteners over 16 to 24 months and three shorter trials showed no effect with artificial sweeteners use over 6 months. Both of the longer-term trials, however, were industry sponsored, and all five trials were at high risk of bias.
- Long term follow up studies however demonstrated modest long-term gains in body weight, BMI, and waist circumference and increased risk of the following conditions: Hypertension by 13 percent, stroke by 14 percent and cardiovascular events by 32 percent. It is however unlikely that those chemicals cause health problems directly. Recent studies have shown artificial sweeteners can disrupt the gut microbiome in rats and adult humans. Thus, routinely consuming artificial sweeteners may be selecting for an obesity promoting microbiome (bacteria in the gut). There is also evidence that routine consumption may confuse and "reprogram metabolism in a way that favors weight gain, insulin resistance, and glucose intolerance, she said. Consuming artificial sweeteners may also promote a sweet tooth or give

- people a sense of "permission" to eat higher-calorie foods because they "saved" on calories with their diet drink. [19]
- Diet soda may also cause stroke and dementia. A 2017 study published in American Heart Association's journal Stroke showed that when 2800 participants were compared to individuals who drank no diet sodas drinks a week, hazard rations for the risk of stroke and dementia were up 3 times respectively. [20]

Fast Food

- Fast food intake results in an immediate increase in blood glucose (sugar) and blood lipids (fat), as well as oxidative stress and inflammation, which leads to fatty plaque buildup in the arteries. [21]
- Eating fast food just once a week can increase an individual's risk of dying from coronary artery disease by 20 percent, and 50 percent if eaten twice a week. This risk rises to 80 percent if fast food is eaten more than four days a week. [22]
- An animal study concluded that mice that ate a high fat diet for two weeks had an increase in myocardial lipid levels (fat in the heart) and reduction of the strength of the heart muscle by 30 percent. [23]
- Meat used by many fast food restaurants has very high nitrogen content. Why? It comes from
 animals that are fed over-fertilized corn and kept in extreme confinement. These conditions
 allow the animal to ingest its own feces and recycle nitrogen. Bon appetite! [24]



What to Eat

When making food choices make sure to use common sense and try foods that didn't exist 100 years ago. If your food originated from the farm, it is most likely good for you, if it came from a plant, which also makes rubber, probably is not a good choice! (Azodiacarbonamide, which is found in products such as yoga mats and shoe leather, was used in the past by Subway to make their bread chewier!) The Mediterranean and Plant-based diets are best choices and are associated with significant reduction in risk of heart disease diabetes, hypertension, stroke, cancer and dementia as well as being demonstrated to lead to regression (reversal) of heart disease.

Defining Serving Size

It is important to know the serving size for the healthy foods you are consuming including fruits, vegetables, grains and meats. These serving sizes are defined as the following:

- Fruits: 1 medium sized fruit (baseball size), ½ cup juice, or ½ cup of cooked or chopped fruit.
- Vegetables: 1 cup of raw vegetables, ½ cup of vegetable juice or ½ cup of other vegetables.
- Grains: ½ cup of cooked rice, pasta or cereal, 1 slice of bread.
- Meat: 2 to 3 oz cooked lean meat or fish (deck of cards).



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Mediterranean Diet: The Best. Period! (And it tastes great as well!)

The traditional diet in the countries surrounding the Mediterranean Sea, including France, Italy, Spain, Morocco, and Greece, was considered a "poor man's" diet, developed over the centuries as people labored to create sustenance in less hospitable terrain. Health experts and nutrition researchers didn't create the Mediterranean diet in a lab. "The Mediterranean diet is a traditional diet that evolved over 5,000 years. The Mediterranean diet has been the subject of intensive research for more than 50 years, ever since Ancel Keys, PhD, a professor from the University of Minnesota, first performed his legendary, post-World War II Seven Countries Study, which examined the health outcomes of nearly 13,000 middle-aged men in the United States, Japan, Italy, Greece, the Netherlands, Finland, and then Yugoslavia. His team found that men from Crete experienced lower cardiovascular disease rates than their counterparts in other countries a link the researchers attributed to the men's postwar "poor" diet, which focused on fruits, vegetables, grains, beans, and fish. Since Keys' first observation decades ago, hundreds of studies have documented an array of health benefits linked with the traditional Mediterranean diet, including increased life span; healthy weight; improved brain function; fewer symptoms of rheumatoid arthritis and poor fertility and eye health; lower risks of certain cancers, heart disease, Alzheimer's disease, and diabetes; and lower levels of blood pressure and LDL cholesterol.

The principal aspects of this diet include proportionally high consumption of olive oil, legumes, unrefined cereals, fruits, and vegetables, nuts, moderate to high consumption of fish (at least twice a week), moderate consumption of dairy products (mostly as cheese and yogurt), moderate wine consumption, and low consumption of non-fish meat products (1-2 times a month).

Mediterranean Diet Health Facts

- A large prospective study published in the New England Journal of Medicine involved population of 7,500 participants who adhered to either Mediterranean diet supplemented with EVOO (extra virgin olive oil), or nuts or a low fat diet. Those who ate the two Mediterranean diets had a 30 percent reduction on combined endpoint death, heart attacks, and stroke compared to a low-fat diet. [25]
- Following a low-carb Mediterranean diet (as opposed to a low-fat diet) may decrease the need for drugs in diabetic patients by 26 percent. [26]
- This diet helps to lower the risk of type 2 diabetes in older adults by 52 percent! [27]
- Even without weight loss, it appeared to decrease the risk of metabolic syndrome (Collection of risk factors for diabetes including abdominal obesity, high blood pressure, and elevated blood pressure and triglycerides).
- The diet also showed a 62 percent lower risk for malignant breast cancer compared to those with a low-fat diet. [28]

- The Mediterranean diet rich in virgin olive oil increases the quantity and function of HDL (good cholesterol). [29]
- A 2016 study of 4,753 participants showed that those who adhered to a Mediterranean diet had the lowest odds of developing neovascular age-related macular degeneration of the eye. [30]
- A 2017 study demonstrated a similar effect: the risk for age-related macular degeneration can be cut by more than one-third by eating a Mediterranean-style diet that is heavy in fruit, vegetables, legumes, whole grains, fish, and lean meats, new data from an ongoing Portuguese study suggest. And these are the first data to conclude that caffeine not traditionally included in the Mediterranean diet but consumed in beverages popular in the region studied. For people who ate the equivalent of just one apple each day, there was a 15 percent decrease in the risk for age-related macular degeneration; for those who ate the equivalent of two apples each day, there was a 20 percent decrease. In addition, macular degeneration was less common in people who consumed the equivalent of one shot of espresso each day than in people who did not (45.1% vs 54.4%). [31]
- A Journal of the American Medical Association study including 90,000 postmenopausal woman concluded that higher adherence to the Mediterranean diet resulted in a lower risk of hip fractures. [32]
- Mediterranean diet can also slow cognitive decline. A study showed that those with the lowest adherence to the diet saw a greater 3-year decline in brain performance. [33]
- In the Nurses' Health Study, greater adherence to the Mediterranean diet was associated with greater telomere length, a biomarker of aging. [34]
- It is even effective for smokers! (you still should quit smoking!!!)
- Among smokers adhering to Mediterranean diet the presence of plaques in the femoral arteries was reduced by 61 percent compared to smokers who did not follow this diet! [35]



Plant-based Diets

- A Plant-based diet aims to increase the nutrientdense plant based food consumed and limits the amount of processed food, oils and animal products eaten. The diet is rich in foods such as vegetables, fruits, nuts, beans, peas and seeds.
- Plant-based is often used interchangeably with vegan and vegetarian. Vegans exclude all animal products from their diet, while vegetarians may include eggs and milk into their diet.



- Studies done have shown that compared to non-vegetarian diets, vegetarians are less likely to be obese and have lower body mass index's. There was an estimated weight difference of 7.6kg for men and 3.3kg for woman.
- A study demonstrated that over a 17-year period, non-vegetarians are 74 percent more likely to develop diabetes than vegetarians.
- Vegetarians have a 24 percent decreased risk in ischemic heart disease death rates. [36]
- Participants eating a plant-based diet with unrestricted food intake lost an average of 25.4lb in one year, decreased waist circumference by 9 cm and decreased hypertension and diabetic medication usage by 29 percent. [37]

Only because you don't eat meat and consider yourself vegan or vegetarian it does not mean you are eating healthy!

A new study suggests that to reduce the risk of coronary heart disease it is simply not enough to eat a plant-based diet but that the foods in that diet must be high quality. After two decades of follow-up in more than 200,000 adults, researchers found that adherence to a plant-based diet rich in whole grains, fruits, vegetables, nuts, and legumes was associated with a substantially lower relative risk of coronary heart disease (25 percent reduction), whereas following a plant-based diet emphasizing less healthy foods such as refined grains and sugar-sweetened beverages (fruit juices instead of fruit) had an adverse effect. (32 percent increase in risk) And here is more good news: occasional red meat consumption did not affect the protective effects of plant based diet! [38]

Are there any possible drawbacks of vegan diet?

In a Japanese study (Ohasama town study) of over 1000 older males higher protein, particularly animal protein, was associated with lower risk of decline in higher-level functional capacity in older men. Animal protein intake may be a modifiable indicator for early detection and prevention of higher-level functional decline in elderly adults. [39]

Components of our Diet

Salt and Sodium: not as evil as doctors are painting it!!!

Sodium is an essential action and is crucial to the action potential of all cells in the body .28 Sodium homoeostasis is under tight physiological regulation. Further, emerging evidence suggests that inflammatory responses with infections involve mobilizing high concentrations of sodium to the local tissues that are involved, and this ability might be part of an essential defense mechanism to external infections. To convert salt to sodium multiply by 0.39.

Statistics

- Salt was introduced to our diet 5,000 years ago by the Chinese to preserve meat and fish.
- Excessive (keep on reading...) salt consumption is linked to high blood pressure, increased risk of stroke, osteoporosis, obesity, stomach cancer, kidney stones, coronary artery disease and vascular dementia.
- In the 1950s, Japan initiated a campaign to lower national salt intake. Over a decade, salt intake was reduced by 25 percent. Results showed blood pressure was reduced as well as a reduction in stroke death by 80 percent
- Similarly, in Finland, salt intake reduced by one-third, resulted in a reduction in blood pressure, 75-80 percent reduction in stroke and coronary heart disease related death and a five to six year increase in life expectancy. [40]

Keep in mind: Japan and Finland had extremely high salt consumption, much higher than the American diet!

Official American Heart Association Sodium Intake Recommendations

• AHA recommends sodium consumption below 2300 mg for adults over age 14, and 1,500 for those with prehypertension and hypertension.

But is there evidence that this recommendation actually works??? Short Answer: No

In a biggest prospective study to date (PURE) investigators studied 133,118 individuals (63,559 with hypertension and 69,559 without hypertension), median age of 55 years and estimated 24-h urinary sodium excretion (as group-level measure of intake rather than relying on patients estimates on salt consumption) Median follow up (duration of observation) was 4.2 years.



The results were rather shocking for individuals with high blood pressure (hypertension) sodium excretion of 7 g/day or more was associated with 23 percent increase risk of cardiovascular events and death but sodium excretion below 3 g resulted in 34 percent increase in cardiovascular events and death! (compared to those hypertensive patients with 4-5 g excretion).

What about individuals without high blood pressure?

High sodium consumption of over 7 g/day was not associated with adverse outcome but restriction to less than 3 g lead to 2^percent increased risk of adverse outcome!

Authors noted that most of the world's population (about 95 percent) studied consumes more than 3 g/day of sodium, regardless of hypertension status and only 22 percent consume 6 g/day or more of sodium the threshold above which we note an increase in mortality and cardiovascular disease risk. [41]

Restaurants are a major source of sodium. Ask a restaurant about low-sodium options on their menu.

Among the saltiest were: [11]

Chili's Boneless Buffalo Chicken Salad	3,730 mg
TGI Friday's Jack Daniel's Ribs & Shrimp	4,140 mg
Cheesecake Factory Sunrise Fiesta Burrito	4,600 mg
Applebee's Sizzling Skillet Shrimp Fajita	5,140 mg
Applebee's Appetizer Sampler	6,260 mg
PF Chang's Hot & Sour Soup Bowl	7,980 mg

By far most of the sodium Americans ingest, nearly 71 percent, comes from foods prepared outside the home, new research indicates. Sodium found naturally in foods consumed accounts for 14 percent, and salt added in the course of preparing food at home amounts to 5.6 percent of intake, it also found. Only 4.9 percent of ingested sodium comes from saltshakers at the table at home. [42]



Potassium

Increasing potassium consumption is more important than restriction sodium intake!

- Increasing consumption to 4.7 g per day (Recommended intake) would lower systolic blood pressure up to 3.2 mm Hg. [43]
- This would reduce your risk of stroke death by eight to 15 percent and heart disease death by six to 11 percent. [44]



- Potassium rich foods include fruits (such as tomatoes, oranges, apricots, and bananas), vegetables, whole grains, dairy products and coffee.
- A 1.64-g per day higher potassium intake was associated with a 21 percent lower risk of stroke.
- This amount of potassium is equivalent to about three pieces of fruit high in potassium and could translate to a reduction of over one million stroke deaths per year worldwide. [45]

Fats

Saturated- Saturated fats are solid at room temperature and have no double bonds. There is a recently lots of confusion and disagreement regarding safety of saturated fats. *Monounsaturated*-liquids at room temperature and contain one double bond. These fats decrease levels of LDL in the blood stream leaving more HDL. Olive, peanut and canola oils are high in monounsaturated fat.

Polyunsaturated-Are also liquid at room temperature but contains two or more double bonds. These fats split into omega-3 and omega-6 and decrease levels of LDL. Walnuts, sunflower seeds, flax seeds and fish are high in polyunsaturated fat.



Diets, which have been demonstrated, to prolong life, prevent stroke and heart disease such as Mediterranean or plant base diet are fairly low (Mediterranean) or very low (vegan) in saturated fats!

In Chapter 1, we presented population with healthiest hearts in the world, the Bolivian Tsimane Indians. Their diet is very low in fat with only 14 percent of their calories being fat calories. This is as low as the traditional Okinawan



population known for longevity as a Blue Zone and in the range of the famous heart disease prevention and reversal studies of Dean Ornish, MD and Caldwell Esselstyn, MD. Their diet was also very low in saturated fat, averaging 11 grams, and had no measurable Trans fats!

Saturated Fat: Good, Bad or Indifferent?

Official Opinion

AHA (American Heart Association) Issues 'Presidential Advisory' on Harms of Saturated Fat (June 2017): [46]

"Replacing saturate with polyunsaturated fats resulted in 30 percent reduction in cardiovascular morbidity and mortality." Replacing saturated fats with "bad carbs": white bread, white rice, pizza crust, hamburger buns cancels however all beneficial effects of eliminating saturated fats. Here is however a minor problem: AHA received founding from makers of vegetable oils: Procter & Gamble, original maker of Crisco as well as Bayer, the owner of LibertyLink soybeans. AHA recommendations are based on decades old, poorly designed studies.

For example one of the evidence quoted was diet-heart study from the 1970s, conducted in Finnish mental hospitals, which was especially poorly controlled. The patients were not randomly assigned and as a result, it was impossible to determine why cardiovascular event rates differed. For instance, the antipsychotic medication thioridazine, which was later found to cause sudden cardiac death, was dispensed disproportionately to the control arm on the regular saturated-fat diet!

"The Alternative Opinion"

There are multiple studies, which do not agree with AHA statement about harm of saturated fat leading to heart disease. One possible explanation is that while it's true that saturated fats drive up LDL cholesterol a bit, they also raise HDL cholesterol, the effect on heart-disease risk. Since 1970, Americans have cut their intake of animal fats by 27 percent while increasing consumption of polyunsaturated vegetable oils by nearly 90 percent. Since the introduction of these oils in the early 1900s, their consumption has risen more than any other foodstuff in America, to almost 8 percent of all calories consumed by the year 2000. Meanwhile, cardiovascular disease remains a leading cause of death among men *and* women. If replacing saturated fats with polyunsaturated fats were the answer, we would see a significant impact on cardiovascular mortality, which is not the case.

- Source of saturated fat also makes a difference: Multi Ethnic Study of Atherosclerosis including 5,000 adults found that eating dairy products high in saturated fatty acids actually decreased risk of coronary artery disease while eating meat high in saturated fat increased risk for coronary artery disease. [47]
- •In a study of 3333 adults observed for over 20 years, comparing people consuming skim milk versus regular milk, researchers discovered much higher risk of type 2 Diabetes Mellitus when skim milk is consumed. People who had the most dairy

fat in their diet had about a 50 percent lower risk of diabetes compared with people who consumed the least dairy fat! [48]

What about butter?

A recent metaanalysis of 9 publications (including 15 country-specific cohorts, together reporting on 636,151 unique participants with 6.5 million person-years of follow-up and including 28,271 total deaths, 9,783 cases of incident cardiovascular disease, and 23,954 cases of incident diabetes) demonstrated that butter had essentially a neutral effect on mortality, heart disease, stroke and diabetes. It is possible that other ingredients in



butter offset negative effect of saturated fats: Branched-chain fatty acids in dairy fat may promote healthier bacterial microbiome composition and function. Dairy fat also contains monounsaturated fats, which might improve glycemic responses and insulin sensitivity. [49]

Coconut saturated fat content is higher beef fat and pork lard

There is a misconception that coconut oil is a healthy alternative to olive oil! This is far from the truth! It is packed with saturated fat, 82 percent of the fat in coconut oil is saturated. That's more than in butter (63 percent), beef fat (50 percent) and pork lard (39 percent). Use it occasionally but your main oil should be Extra Virgin Olive Oil! [50]



The End of "The Fat and the Heart disease story"

The Prospective Urban Rural Epidemiology (PURE, published in August 29 2017) study is a large epidemiological cohort study of individuals aged 35–70 years in 18 countries with a median follow-up of 7.4 years. Dietary intake of 135,335 individuals was recorded using validated food frequency questionnaires. During follow-up, there were 5796 deaths and 4784 major cardiovascular disease events. This study finally killed the conventional recommendation to eliminate fat from diet. Not only dietary fats did not cause cardiovascular issues but tend to prevent them! Results below compare individual sugar and fat intake in the top quintile (top 20%) versus bottom quintile (bottom 20%)

Higher carbohydrate intake was associated with a 28 percent increased risk of total mortality. Intake of total fat. When broken down into individual fat types, mortality was reduced by 14 percent for saturated, 19 percent monounsaturated and 20 percent polyunsaturated. Saturated fats decreased risk of stroke by 21 percent. Total fat and saturated and unsaturated fats were not significantly associated with risk of myocardial infarction or cardiovascular disease mortality. [51]

Author's verdict regarding saturated fat:

Moderation is the key

It's the sugar, stupid!

Bulletproof coffee (new trend with added butter and coconut oil): probably not the best idea to drink 1000 calories for breakfast!



Trans Fats

Trans-Mostly formed artificially but can be found in meat and dairy products in small amounts. These fats not only increase LDL but have been associated with heart disease and stroke. Only "synthetic" trans-fats are toxic!

• Trans-fat is a tragic story for the American diet. In the 1950s and '60s, Americans were told that butter and eggs were bad for them and pushed people to margarine, which is basically trans-fat. Now we know is that saturated fat is relatively



neutral it is the trans-fat that is really harmful and we had made the dietary situation worse

List of most common foods containing trans fats (All trans fats will be phased out by 2018)

- 1. Cakes, pies and cookies (especially with frosting)
- 2. Biscuits
- 3. Breakfast sandwiches
- 4. Margarine (stick or tub)
- 5. Crackers
- 6. Microwave popcorn
- 7. Cream-filled candies
- 8. Doughnuts
- 9. Fried fast foods
- 10. Frozen pizza



Source: Kristin Kirkpatrick, MS, RD, LD, Cleveland Clinic Wellness Institute

• From 2007-2011 New York State put a ban on 11 counties restaurants from cooking with transfats. When comparing hospitalizations to the counties without the ban, banned counties had a 7.8 percent decline in heart attack and a 3.6 percent decline in stroke events. [52]

• For every 2 percent of calories consumed from trans- fats daily, you have an increased risk for heart disease by 23 percent. [53]

Trans Fats Shrink the Brain and Increase Dementia Risk

• Study involving 104 elderly participants published in the medical journal Neurology, found a diet high in trans fats shrinks the brain and increases a person's risk of developing dementia symptoms. [54]

Dietary Cholesterol [55]

2015 dietary guidelines no longer restrict dietary cholesterol intake.

- For most people, the amount of cholesterol eaten has only a modest impact on the amount of cholesterol circulating in the blood. [56]
- For approximately 30 percent of people, blood cholesterol levels rise and fall very strongly in relation to the amount of cholesterol eaten. For these "responders," avoiding cholesterol-rich foods can have a substantial effect on blood cholesterol levels. Unfortunately, at this point there is no way other than by trial and error to identify responders from non-responders to dietary cholesterol.

What about eggs?

• In studies of more than 80,000 female nurses, Harvard researchers found that consuming about an egg a day was not associated with higher risk of heart disease. [57]

Great news for diabetic patients as well!

In a large prospective study (PREDIMED) lasting almost 6 years low to moderate egg consumption (up to 4 eggs per week) was not associated with an increased CVD risk in diabetic or non-diabetic individuals at high cardiovascular risk. [58]

Does it mean I can have eggs every day?

No, as daily egg consumption changes bacterial flora leading to TMAO production and atherosclerosis, but 4-5 x a week does not seem to be a problem!



Dietary Fiber

- There are two types of dietary fiber: soluble and insoluble. None of them is digested in our body. It remains the same from plate to toilet.
- Soluble fiber can dissolve in water, jellifies stomach content and helps moderate blood glucose levels (by slowing down absorption) and lowers cholesterol. Soluble fiber includes oats, legumes, fruits and vegetables.



• Insoluble fiber does not dissolve in water making waste heavier and softer so it can shimmy trough the intestine more easily. Insoluble fiber is high in whole grain and wheat bran.

What is the recommended fiber intake?

- According to the Institute of Medicine (IOM) (2002), dietary reference intake (DRI), an adequate intake for total fiber, is set at 38 and 25 gram (g) per day for young men (age 14-50 years) and women (age 19-50 years), respectively. Adults over 50 require less fiber (30 g for males and 21 g for females).
- Simple way to increase fiber content in your meal is to add ground flaxseed (2 tablespoons contain 3.8 g of fiber) or Chia seeds (5.5 g of fiber per tablespoon).
- A study of over 200,000 men and 150,000 women found that dietary fiber intake was associated with a 12 percent reduction in total mortality in both men and women.
- Fiber decreased the risk of death from cardiovascular, infectious and respiratory diseases. (Lowered by 24 56 percent in men and by 34 59 percent in women).
- There was an inverse association between dietary fiber intake and death caused by cancer. [59]

GREAT HIGH FIBER FOODS









PEAS FIBER 8.8 G. PER CUP,COOKED

BRUSSELS SPROUTS FIBER 4.1 G. PER CUP,BOILED

ARTICHOKES
FIBER 10.3 G.
PER MEDIUM VEGETABLE, COOKED

BROCCOLI FIBER 5.1 G. PER CUP, BOILED











BLACK BEANS FIBER 15 G. PER CUP, COOKED

BLACKBERRIES FIBER 7.6 G. PER CUP,RAW

LENTILS
FIBER 15.6 G.
PER CUP,COOKED

PEAR
FIBER 5.5 G.
PER MIDIUN FRUIT, RAW

LIMA BEANS FIBER 13.2 G. PER CUP, COOKED











AVOCADO FIBER 7.6 G. PER HALF,RAW

RASBERRIES FIBER 8 G. PER CUP, RAW

BRAN FLAKES FIBER 7 G. PER CUP, RAW

WHOLE-WHEAT PASTA FIBER 6.3 G. PER CUP,COOKED

PEARLED BARLEY FIBER 4 G. PER CUP, COOKED

Superfoods

Eat these foods daily!

Dark Greens

- Leafy greens are high in fiber, vitamin C, folic acid, potassium and magnesium and are low in fat. This provides nutrition to your microbiome! (Beneficial bacteria living in the gut).
- Dark leafy green vegetable consumption can lower your risk for stomach, skin and breast cancer and heart disease and diabetes. [60]



Extra Virgin Olive Oil: The Magic Ingredient of Mediterranean Diet

Cardiovascular:

 A study showed that participants who consumed the most olive oil reduced the risk of cardiovascular disease by 35 percent and mortality by 48 percent. Cardiovascular disease and mortality decreased by 10 percent and 7 percent respectively for each 10g/d increase in consumption. [61]



• Extra virgin olive oil increases HDL levels (good cholesterol) and lowers blood pressure.

Brain:

- In a study of 12000 participants daily olive oil consumption reduced significantly risk of depression. [62]
- Initial studies have shown that an olive oil extract (oleocanthal) may help protect you from the risk of Alzheimer's disease and cognitive decline. [63]

Bone:

• Published evidence suggests that olive oil phenols can be beneficial by preventing the loss of bone mass. It has been demonstrated that they can modulate the proliferative capacity and cell maturation of osteoblasts (cells creating new bone tissue) by increasing alkaline phosphatase activity and depositing calcium ions in the extracellular matrix. [64]

Inflammation:

• Olive oil has potent anti-inflammatory effect in acute and chronic inflammation: 3.5 tablespoon dose is equal to a 200mg tablet of ibuprofen. [65]

Berries

- Strawberries and blue berries may prevent hypertension. A blood pressure reduction of 8 percent in those with highest intake was found. Those who saw the greatest benefit were under 60 years old (12 percent reduction in blood pressure observed). [66]
- In a 2013 Nurses' Health's Study II, 93,600 women consuming a berry enriched diet were followed for 18 years. Results showed a 1/3 reduction in myocardial infarction when more



than 3 servings of strawberries and blueberries were consumed per week. This reduction may be due to the flavonoid, anthocyanin as it exerts anti-inflammatory effects on the heart. This causes beneficial effects on the heart by improving endothelial function and blood pressure. [67]

- A 2012 study with 1600 participant's study confirmed that eating berries at least once a week could slow cognitive decline by 1.5 to 2.5 years. [68]
- The more fruits and vegetables the better!
- 200g of vegetables and fruit can decrease risk of heart disease and cancer by 13 percent and 4 percent respectively. 800g decreases risk by 28 percent and 13 percent. [69]

Avocados

- For people who are overweight and obese, eating one avocado a day can help improve LDL (bad) cholesterol levels.
- A 2015 study looked at 45 healthy overweight or obese participants separated into three diet groups after eating an American diet for two w. The diets included low-fat, moderate fat and avocado diet. Results showed that avocado diet had largest reductions of LDL cholesterol by 22 percent and increase HDL by 11 percent, Of interest avocado targeted one particularly nasty (small dense LDL particle) responsible for plaque buildup! [70]
- Avocados are rich in vitamins B, C and K and contain more potassium than bananas.

• Avocados have an average of 200-300 calories per serving (take this in consideration!)

Avocados are becoming increasingly more popular to the point of fueling crime...

Here are few news headlines:

Trio charged with \$300,000 avocado theft...

New Zealand avocado thefts grow as demand surges...



Fish

Eat minimum two serving of salt water fish twice a week. Best source of omega 3 is oily fish such as salmon, mackerel, sardines, herring and anchovies. Canned fish is ok as well!

Don't like fish?

You can replace it with frequent consumption of walnuts and flax seed meal.



- Consuming one serving of fish per week is associated with a 17 percent decreased risk of coronary heart disease death. Each additional serving of fish per week decreased risk another 4 percent.
- Fish are high in omega-3 fat and can help to reduce inflammatory markers, and therefore also fatty plaque build-up in arteries. [71] These omega-3 fatty acids reduce overall and cardiac death in patients with heart disease by 32 percent. [72]
- Eating fish can reduce the risk of atrial fibrillation, an abnormal heart rhythm, more common in the elderly. [73]



- A study published in JAMA showed the association between seafood consumption and Alzheimer's disease. After looking at 286 autopsied brains, the study concluded that moderate seafood consumption correlated with less Alzheimer's neuropathy. [74]
- Eating fish reduced activity of rheumatoid arthritis: when fish was consumed >2 x a week the magnitude of the effect, was quite impressive: about one-third of the expected magnitude of the standard drug treatment of rheumatoid arthritis with methotrexate. [75]

Salmon: wild or farmed?

• Farmed salmon contains more omega-3 fatty acids than wild salmon. One three ounce serving of good quality farmed salmon contains 2g of omega-3 fatty acids compared to 1.4g in wild salmon. The problem is that omega 3 content of farmed salmon varies depending on feed: fish pellets and seaweed increase omega 3 but soybean based feed increases mainly saturated fat.



Origin of farmed salmon matters as well!

In past several years Chile experienced problems with a bacteria known as SRS, or Piscirickettsiosis. The bacteria causes lesions and hemorrhaging in infected fish, and swells their kidneys and spleens, eventually killing them. This resulted is record use of antibiotics!

In 2014, the industry produced around 895,000 tones of fish and used 563,200 kilograms (1.2 million pounds) of antibiotics, according to government and industry data. In contrast, Norway, the world's largest salmon producer, produced around 1.3 million tones of fish and used 972 kilos of antibiotics in 2013.

Issue of artificial coloring in farmed Salmon (or rather no issue)

Artificial color is added to make the flesh of the salmon pink rather than gray. The reality is that the chemical used to color the salmon, astaxanthin, is a manufactured copy of the pigment that wild salmon eat in nature, which gives wild salmon their pinkish-red color. No worry here!



Author's Verdict

Both wild and farmed salmon are an excellent choice. Avoid however Chilean salmon (Kroger, Walmart, Sam's Club) and choose Nordic or Icelanding antibiotic free fish instead (Costco, Wholefoods). Even better news: Since Amazon acquired Wholefoods, the price of Icelanding is down to \$9.99!



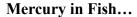
Please don't fry me! I died once already!

Frying fish kill its benefits!!!

• When fish is fried, it loses 70-85 percent of its omega-3 fatty acids. [76]

Deep-frying makes it toxic....

• In a large study of 16,479 participants free of heart disease at the onset of the study which lasted 5 years, fried fish intake of two or more servings per week was associated with a 60 percent increased risk of cardiovascular events. Given the increased intake of fried fish in the stroke belt and among African Americans, these data suggest that dietary fried fish intake may contribute to geographic and racial disparities in CVD. [77]



- Mercury enters our rivers and oceans through coal burning and mining and other anthropogenic sources. Fish then ingest the mercury. Mercury levels increase up the food chain through biomagnification. (Bigger fish eating smaller fish) Good news is that due to recent worldwide closure of coal power plants mercury levels in fish started decreasing!
- Typical dietary mercury levels have not been shown to raise cardiovascular disease, coronary heart disease or stroke risk. [78]
- However, results do not change public health efforts to decrease mercury contamination of fish and the environment, as mercury can cause neurological effects, especially in children when consumed by pregnant or nursing mothers.
- Examples of fish with the least mercury include: flounder, herring and salmon. Fish with the highest mercury content include orange roughy, tuna (Bigeye, Ahi), and swordfish.
- To view the whole list of fish and their mercury content level you can visit The Smart Seafood Buying Guide. (https://www.nrdc.org/stories/smart-seafood-buying-guide) [79]





What about catfish and tilapia? It is just fine as long as you don't fry it!!!

• Since 2000, catfish and tilapia rank as two of the most popular fish consumed in the United States thanks mainly to their taste and relatively low expense. They contain both the very beneficial omega 3 and less beneficial omega-6 fatty acids. Like omega-3s, these are polyunsaturated and help lower blood cholesterol levels, however they are thought to play a role in clotting function, are pro-inflammatory and susceptible to oxidation thereby possibly increasing risk for blood clots, arthritis, inflammatory bowel disease and cancers. 3-ounce portion of catfish or tilapia contains 67 and 134 milligrams respectively of the bad fat (the same amount of 80 percent lean hamburger contains 34 milligrams, and bacon 191 milligrams). [80]

So, should we stop eating it?

No, it is likely not as beneficial as salmon, mackerel or sardines (with high omega 3 content) and as long as you eat other fish than tilapia and catfish you are ok! As a matter of fact, 2009 statement by American Heart Association clearly concludes that benefits of Omega 6 outweigh any risks and it should be part of our diet! "Aggregate data from randomized trials, case-control and cohort studies, and long-term animal feeding experiments indicate that the consumption of at least 5 percent to 10 percent of energy from omega-6 PUFAs reduces the risk of CHD relative to lower intakes. The data also suggest that higher intakes appear to be safe and may be even more beneficial (as part of a low–saturated-fat, low-cholesterol diet). In summary, the AHA supports an omega-6 PUFA intake of at least 5 percent to 10 percent of energy in the context of other AHA lifestyle and dietary recommendations. To reduce omega-6 PUFA intakes from their current levels would be more likely to increase than to decrease risk for CHD." [81]

If you are really adventurous try fermented herring (Surströmming)! The smelliest food on Earth!!!!

Small Baltic herring are caught in the spring, salted and left to ferment (I would use the word "rotten") before being stuffed in a tin about a month before it sold. The fermentation process continues in the tin, results in a bulging of the tin. You never open the can in the house! (unless as a prank!) and yes you can get it on Amazon.

Not even the Swedes can open the can without vomiting!

Watch this YouTube video before consuming it! (https://www.youtube.com/watch?v=wmu7bHj81WI)

Ground Flax Seed

- Flaxseed has been identified as a major source of omega 3-fatty 3 fatty acid alpha-linolenic acids (ALA) that differ from that of fish.
- Nine studies have shown that ALA is inversely related to cardiovascular events.
- ALA found in flaxseed is associated with a decreased risk of recurrent fatal and nonfatal myocardial infarction and a 73 percent decreased risk of cardiac morbidity and mortality.
- Increasing flaxseed consumption can decrease the risk of stroke by 28-37 percent.
- A study in which postmenopausal woman consumed 30g of flaxseed per day showed a decrease in LDL cholesterol by 10 percent and total cholesterol by 7 percent. [82]
- A group of individuals who ate 30g of ground flaxseed a day for a year. After 6 months average systolic blood pressure was 10 mm Hg lower and diastolic blood pressure was 7mm Hg lower. [83]

Dark Chocolate

- In a study of nearly 20,000 participants, those who reported their chocolate intake in the top quarter of participants had a 27 percent reduced risk of heart attack and nearly a 50 percent reduced risk of stroke. [84]
- Eating 1 oz of dark chocolate per day for two weeks can reduce blood pressure and LDL cholesterol levels.
- These benefits are likely from flavanols. [85] Flavanols release nitric oxide in the endothelium (thin layer of cells that lines blood vessels), leading to lower blood pressure and better platelet function.
- In a study of more than 31,000 women, the risk of heart failure over nine years declined 26 percent for women who reported a monthly chocolate intake of one to three servings and by 32 percent for those who said they are one or two servings per week. [86]
- Effects are accomplished with SMALL amounts of dark chocolate! [82] Moderation is important as chocolate contains a lot of calories and fat. (limit to 1 oz).
- The reversal of vascular dysfunction is comparable to treatments such as exercise and medications (including insulin and ACE inhibitors), mostly due to the presence of flavanols.



- Antioxidants in cocoa benefit conditions linked to oxidative stress such as lung disease, atherosclerosis, heart failure, heart attack and some cancers. [87]
- A significant reduction in insulin resistance (a condition when insulin becomes less effective at lowering blood sugars) was also seen.
- Many studies have linked intake of chocolate, especially flavanol-rich dark chocolate, to improved blood pressure and other cardiovascular benefits. [86]
- Cocoa flavanols can improve tobacco induced endothelium (inner lining of an vessel) damage by enhancing production of nitrous oxide, (laughing gas) smoking. [88]
- Flavanols show beneficial effects on LDL, platelet aggregation, insulin sensitivity, endothelial function and blood pressure. [85]
- A 2010 study looked at 19,357 participants and tracked chocolate consumption and incident cases of heart attack and stroke. Results showed that those who ate the most chocolate had a 27 percent reduction in heart attack risk and the risk of stroke by 48 percent. [84]
- A 2005 study compared the effects of dark chocolate vs. white chocolate on blood pressure. 15
 participants ate either dark or white chocolate for 15 days and results showed that cholesterol
 and blood pressure were reduced after dark chocolate consumption compared to white
 chocolate. [89]
- One study concluded that just after two hours of ingesting 40g of dark chocolate, the participants had significantly increased maximal walking distance and maximal walking time compared to those who ingested milk chocolate. [90]
- A 2016 study concluded that chocolate consumption is associated with better cognitive performance when habitual chocolate consumption participants had better performance on the Global Composite score, Visual-Spatial Memory and Organization, Working Memory, Scanning and Tracking, Abstract Reasoning, and the Mini-Mental State Examination. [91]
- Dark chocolate reduced risk of atrial fibrillation (common arrhythmia especially in elderly, leading cause of stroke). In a study of 55,502 participants observed over 13.5 years, moderate chocolate consumption defined as 2-6 servings per week reduced risk of atrial fibrillation by 20 percent.

Is Dark Chocolate safe for patient with Diabetes?

For people with type 2 diabetes, daily dark chocolate consumption of 20 grams per day (that was rich with polyphenols) helped increase the sensitivity to insulin. This is important for blood glucose control. Increasing insulin sensitivity may also help delay the onset of type 2 diabetes in people with pre-diabetes. [92]



For those who are not chocolate lovers.....

375 mg of flavonoids per serving without fat and sugar (made by Mars).

Mars together with Harvard Medical School started research protocol to establish benefits of flavonoid supplements. This randomized placebocontrolled trial, called the Cocoa Supplement and Multivitamin Outcomes Study (COSMOS), will enroll 18,000 women and men nationwide, making it the largest dietary intervention study to evaluate the health benefits of cocoa flavanols and a multivitamin. (Enrollment ends in 2020). Mars is providing financial infrastructure support together with the Heart, Lung and Blood Institute of the NIH, as well as the cocoa flavanol-containing capsules for use in this trial. The capsules are prepared specifically for research purposes and are produced using Mars' proprietary Cocoapro process to extract flavanols from cocoa beans. Stay tuned



tuned

Not all chocolates are created equal!

for results.

- Look for preferably more than 70 percent cocoa content and no added sugar. For more information check out: (https://healthyeater.com/dark-chocolate-best-and-worst)
- When researchers at the University of Leeds in the UK analyzed 12 common brands of dark chocolate, they found that the flavanol content ranged widely from brand to brand: from as little as 90 mg to as much as 900 mg per serving. 200 mg of cocoa flavanols a day is what it takes to reap the heart-health benefits, but because the flavanol content varies so widely in most chocolates, consumers cannot guarantee a health benefit from all products.

What about weight gain from chocolate? Thankfully the answer is: No!

- In a study of 1,000 people with average age was 57, investigators found that those who ate chocolate the most often had lower BMIs (Body mass index) than the others, even after adjusting for other factors such as age, gender, education and fruit and vegetable consumption.
- For the typical person, the difference between frequently eating or infrequently eating chocolate could account for a 5 to 7-pound difference.
- The findings certainly were not explained by the chocolate eaters eating fewer calories. They ate more calories and didn't exercise more either! [93]

Nuts

- Consumption of nearly any kind of nut improves blood lipid levels, lowers total and LDL cholesterol levels and improves other important lipid ratios. Total cholesterol was reduced by 5.1 percent, and LDL cholesterol levels were reduced by 7.4 percent. [94]
- Diets enriched in a variety of nuts reduce total and LDL cholesterol by 5 to 15 percent. [95]



- A number of studies found that the more nuts a
 person consumes, the less likely they are to die, especially from diseases such as heart disease
 or cancer.
- Recommended amount is 1 oz a day. People who eat this amount of nuts reduce their risk for coronary artery disease by 29 percent, cardiovascular disease by 21 percent and cancer by 15 percent. [96]
- Nuts can also reduce the risk for respiratory disease by 52 percent, diabetes by 39 percent, and infectious disease by 75 percent. [96]
- One study showed that women who consumed more nuts during pregnancy were least likely to have children with nut allergies. [97]
- Most people believe that nuts are high in fat and make you gain weight. But this is in fact not true! A study found that nut consumers often weighed less than nonconsumers! This may be because nuts are high in fat and protein, so it reduces snacking on other carbohydrates and sugars. [95]

Walnuts

- A diet enriched with walnuts improved endotheliumdependent vasodilation (widening of blood vessels) compared to a diet rich in olive oil.
- A diet including 1.5 ounces of walnuts per day, as a part of a diet low in saturated fat and cholesterol, also helped to reduce cholesterol levels. [86]
- Walnuts are particularly high in omega-3 fatty acids.



Walnuts trigger weight loss

Obese patients consumed on five consecutive days, either a smoothie containing 48 grams of walnuts (1.7 ounces, or about 14 walnut halves and 315 calories) or a placebo smoothie identical in taste and calorie content. Then, after a month on their regular diet, the patients returned for a second five-day trial, with placebo drinkers on the first trial receiving a walnut smoothie, and vice versa.

The participants underwent M.R.I. brain exams while looking at pictures of high-fat food (cake, for example), low-fat food (vegetables) or neutral pictures of rocks and trees.

The study found that when people looked at pictures of high-fat food, activation in the insula, a part of the brain involved in appetite and impulse control, increased among those who drank the walnut smoothie, but not among placebo drinkers.

Walnuts can alter the way our brains view food and impact our appetites! [98]

Peanuts

- Peanuts contain a variety of substances with cardiovascular disease risk reducing properties such as mono-saturated fatty acids magnesium, folate, copper, arginine and fiber.
- They can help to lower triglyceride levels by as much as 24 percent. [87]

Almonds

• Significant reductions in LDL cholesterol have been seen by eating almonds. [91]

More Healthy Choices...

Whole Grain Cereal

- In a study of more than 21,000 men, a high intake of whole grain cereal was associated with lower risk of heart failure.
- With increased whole grain cereal servings per week, heart failure risk decreased.
- The hazard ratios (risk levels) began at 1.0 for 0 servings and were reduced all the way to 0.71 for seven or more servings, with a consistent trend along the way. [99]





Psyllium Fiber

- Supplementing low-dose statin therapy (cholesterol lowering drugs) with psyllium fiber can further lower LDL cholesterol levels.
- In a study using Metamucil as the psyllium fiber source, the combined treatment reduced LDL more than the drug therapy alone; results were equivalent to doubling the drug dosage. [100]

Oranges

 Oranges help to reduce blood pressure in young adults. Participants saw a 4.66 mmHg lower systolic BP and a 6 mmHg lower diastolic blood pressure. [101]



Grapefruit

- Grapefruit can lead to significant decreases in total and LDL cholesterol levels. A 2006 study with 28 healthy adults showed a decrease in total and LDL-cholesterol levels by 8percent in just 9 weeks! [102]
- It also contains flavonoids that prevents coronary atherosclerosis (fatty deposits in arteries).
- Red grapefruit can help to lower triglycerides. [103]
- Grapefruit is not compatible with many medications as it may increase the blood concentration of medication to a dangerous level; please check with your pharmacist!



Here are some examples:

- High cholesterol: Atrovastatin, Lovastatin and simvastatin
- High blood pressure: Felodipine, Nifedipine and Nimodipine
- Heart arrhythmia: Amiodarone, Multaq, and Quinidine
- Antiplatlet agents: Brilinta and Plavix
- Anticoagulation agents: Apixaban and Xarelto

Cinnamon and Cloves

- Taking the equivalent of one to two cloves per day improves cardiovascular and diabetes risk factors.
- Compounds in cinnamon and cloves called polyphenols increase two key components in insulin function:
 - an insulin receptor
 - a molecule that blocks inflammatory responses.
- Polyphenols also work as antioxidants, which are very important in cardiovascular disease prevention. [104]

What does it mean "whole grain"?

THE BRAN

The bran is the multi-layered outer skin of the edible kernel. It contains important antioxidants, B vitamins and fiber

THE GERM

The germ is the embryo which has the potential to sprout into a new plant. It contains many B vitamins, some protein, minerals, and healthy fats.

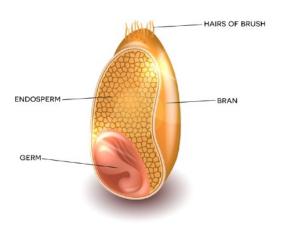
THE ENDOSPERM

The endosperm is the germ's food supply, which provides essential energy to the young plant so it can send roots down for water and nutrients, and send sprouts up for sunlight's photosynthesizing power. The endosperm is by far the largest portion of the kernel. It contains starchy carbohydrates, proteins and small amounts of vitamins and minerals.

Whole grains or foods made from them contain all the essential parts and naturally-occurring nutrients of the entire grain seed in their original proportions. If the grain has been processed (e.g., cracked, crushed, rolled, extruded, and/or cooked), the food product should deliver the same rich balance of nutrients that are found in the original grain seed.

This definition means that 100 percent of the original kernel all of the bran, germ, and endosperm must be present to qualify as a whole grain.

ANATOMY OF A GRAIN



The following, when consumed in a form including the bran, germ and endosperm, are examples of generally accepted whole grain foods and flours.

- Amaranth
- Barley
- Buckwheat
- Corn, including whole cornmeal and popcorn
- Millet
- Oats, including oatmeal
- Quinoa
- Rice, both brown rice and colored rice
- Rye
- Sorghum (also called milo)
- Teff
- Triticale
- Wheat, including varieties such as spelt, emmer, farro, einkorn, kamut, durum and forms such as bulgur, cracked wheat and wheatberries
- Wild rice

"Refined grain" is the term used to refer to grains that are not whole, because they are missing one or more of their three key parts (bran, germ, or endosperm). White flour and white rice are refined grains, for instance, because both have had their bran and germ removed, leaving only the endosperm. Refining a grain removes about a quarter of the protein in a grain, and half to two thirds or more of a score of nutrients, leaving the grain a mere shadow of its original self.

- Since the late 1800s, when new milling technology allowed the bran and germ to be easily and cheaply separated from the endosperm, most of the grains around the world have been eaten as refined grains. This quickly led to disastrous and widespread nutrition problems, like the deficiency diseases pelagra and beri-beri.
- In response, many governments recommended or required that refined grains be "enriched." Enrichment adds back fewer than a half dozen of the many missing nutrients, and does so in proportions different than they originally existed. The better solution is simply to eat whole grains, now that we more fully understand their huge health advantage. Adopted from wholegrainscouncil.org. Look for bread that is whole wheat, preferably with visible seeds and kernels!



Is Gluten really bad for your heart?

- Recent fads have made people believe gluten-free diets are healthier than eating gluten. This is not the case.
- Gluten-free foods offer less protein, but similar amounts of sugar and sodium as foods containing gluten.
- Long-term gluten dietary intake is not associated with coronary artery disease.
- In the Health Professionals Follow-up Study, 64,714 females and 45,303 men were observed from 1986 to 2010 to looked at the association between gluten consumption and coronary artery disease. Results found that a gluten-free diet increases your risk of heart disease by 15 percent. [105]

Beverages

Water, of course!

Water helps your body:

- Keep your temperature normal
- Lubricate and cushion joints
- Protect your spinal cord and other sensitive tissue
- Get rid of wastes through urination, perspiration, and bowel movements

Your body needs more water when you are:

- In hot climates
- More physically active
- Running a fever
- Having diarrhea or vomiting

Pointers

Choose water instead of sugar-sweetened beverages. This can also help with weight management. Substituting water for one 20-ounce sugar sweetened soda will save you about 240 calories. For example, during the school day students should have access to drinking water, giving them a healthy alternative to sugar-sweetened beverages. Choose water when eating out. Generally, you will save money and reduce calories. Add a wedge of lime or lemon to your water. This can help improve the taste and help you drink more water than you usually do. [106]



How much water to drink?

Many people are convinced that they're in a continuous state of dehydration and are concerned about falling short of the 8×8 (eight glasses of 8 oz.) rule. In reality, most people actually consume quite a lot of water each day, just not in the form of pure water. Total water intake including all forms of beverages (water, coffee, tea, soda, and juice) keep us very well-hydrated. In addition, the moisture content in the foods we consume contributes significantly to our daily total water intake. Where did the 8x8 rule came from? This 8×8 rule likely originated from a misinterpretation of an outdated recommendation from 1945 when the Food and Nutrition Board currently part of the Institute of Medicine (IOM) suggested that an individual consumes one milliliter (ml) of water per each calorie of food eaten. Thus, an average diet of 1,900 calories per day would dictate an intake of 1,900 ml (approximately 64 ounces) of water. However, people interpreted this as a recommendation to drink 1,900 ml of pure water, forgetting the fact that water is also found in abundance in the other liquids and foods we consume!

Currently, the IOM liberally recommends an even higher volume of total daily water intake: 3.7 liters (15 cups) for the average adult male and 2.7 liters (11 cups) for the average adult female. If these numbers seem overwhelming, don't panic. Keep in mind that water needs vary significantly by individual, and are dependent on multiple factors such as level of physical activity, geographic location, and temperature. In fact, most people will be adequately hydrated at levels well below these recommended volumes.

Are there advantages of following the 8x8 rule?

A 2002 study published in the American Journal of Physiology and a 2008 study from the Journal of the American Society of Nephrology demonstrated no significant health benefit of the 8×8 rule. However, adequate water intake is still necessary for maintenance of bodily functions.

Practical advice on water intake

So how do you know if your body is properly hydrated? There is really no need to religiously count every ounce of fluid intake! IOM advises drinking liquids (preferably water) with meals and to make sure you listen to your body by drinking when you feel thirsty. This, under most circumstances, will provide you with complete daily water needs. Most people (without specific health issues affecting water balance) will be able to maintain good hydration by following this advice! [107]

Common Misconceptions regarding dehydration

Thirst Is Too Late

It is often stated that by the time people are thirsty, they are already dehydrated. On the contrary, thirst begins when the concentration of blood (an accurate indicator of our state of hydration) has risen by less than two percent, whereas most experts would define dehydration as beginning when that concentration has risen by at least five percent.

Dark Urine Means Dehydration

At normal urinary volume and color, the concentration of the blood is within the normal range and nowhere near the values that are seen in meaningful dehydration. Therefore, the warning that dark urine reflects dehydration is alarmist and false in most instances. [108]

Got Milk?

- Dairy is important part of our diet as it provides us with the main source of calcium. Cow's milk is the best source of calcium, but if fortified, almond and soy milk may be a source.
- Adults should be consuming 700 mg of calcium a day, while adolescents age 11-18 need 1000 mg.
- Full fat and low-fat dairy were associated with 9 percent reduced risk of stroke. [109]
- Circulating levels of trans-palmitoleic acid found in milk are associated with a lower risk of new onset diabetes.
- In a study of more than 3,500 people, circulating trans-palmitoleic acid levels were measured. [110]
- Levels that were less than one percent of total fatty acid strongly correlated with markers of dietary fat consumption.
- Higher levels were associated with higher HDL levels, lower triglyceride levels, lower total/LDL cholesterol levels, less insulin resistance and three-fold lower risk for diabetes.
- Researchers discovered much higher risk of type 2 Diabetes Mellitus when skim milk is consumed. People who had the most dairy fat in their diet had about a 50 percent lower risk of diabetes compared with people who consumed the least dairy fat!

Coffee lovers rejoice!

In <u>EPIC</u> (European Prospective Investigation into Cancer and Nutrition), a large, prospective cohort study, investigators examined the association of coffee intake with all-cause and cause-specific mortality among 451,743 participants (130,662 men and 321,081 women) in 10 European countries. Study lasted 16.4 years. Men who drank three or more cups of coffee per day had a 12 percent lower all-cause mortality than non–coffee drinkers, women had a 7 percent lower mortality.



In terms of cause-specific mortality, men who drank three or more cups of coffee per day had a 59 percent lower risk for digestive disease mortality than men who drank no coffee or less than one cup per day. Women who drank three or more cups had a 40 percent reduction in risk. In women (but not men) risk of death from heart disease decreased by 22 percent and stroke by 30 percent. The mortality benefit was the same for caffeinated and decaffeinated coffee!

Coffee and Inflammation

• After a two-month study in which participants drank four cups a day for one month, and eight cups a day for the 2nd month, there were decreases in markers of inflammation (in the cardiovascular system), as well as increases in HDL cholesterol levels. [111]

Coffee and Diabetes

- Increasing coffee consumption by more than a cup a day over a four-year period reduced type 2 diabetes risk by 11 percent. [112]
- A study even showed that decreasing your coffee consumption by more than a cup a day actually increased their risk for type 2 diabetes by 17 percent. [112]

Coffee and Arrhythmia (irregular heart rate)

Drinking a moderate amount of coffee does not trigger heart rhythm problems. In fact, a 2014 meta-analysis showed that caffeine consumption may actually reduce atrial fibrillation. Atrial fibrillation risk decreased in habitual caffeine consumers by 6 percent for every 300mg/d. [113]

- A 2015 study looked at the consumption of healthy caffeine products including coffee, tea and chocolate. 1,414 participants who consumed these caffeinated products wore a 24-hour Holter monitor (which monitors electrical function of the heart for 24 hours). Results showed no relationship between these compounds and heart rhythm issues. [114]
- It is important to know that these effects come from the antioxidants in caffeine and not the caffeine. Caffeine containing sugar and diet sodas do not have the same effect (just the opposite).

Beetroot Juice

- The nitrate content in beetroot juice can help to lower blood pressure by >10mm Hg. Effects was seen in just 6 hours! [115]
- Nitrates have an advantage over antioxidants: they are not destroyed upon cooking. [116]
- Beetroot juice (about 2/3 cup) can also increase muscle power by 13 percent in those with systolic heart failure (weak heart muscle). The effect was seen in 20 minutes! This is the equivalent of 2-3 months of training in the gym! [117] (but don't skip the gym)



Where to get beetroot juice?

Make your own, or use beetroot powder or beetroot concentrate available online.

Pomegranate juice

- Daily consumption for three months. Significantly improved coronary blood flow. (Blood supplying heart muscle).
- Pomegranate juice lowers blood pressure.
- It may have properties that counter plaque build-up, by substances such as cholesterol, in the arteries. [118]



Cranberry juice

- Cranberry juice helps increase HDL cholesterol; a 10 percent increase observed in studies translated to a 40 percent reduction in risk for heart disease.
- It also aids in decreasing body weight and body mass index. [119]



Tea

- Drinking one or more cups of tea a day has been associated with a reduced risk of cardiovascular events and reduced progression of coronary artery calcium. [120]
- A green tea extract reduces both total and LDL cholesterol. [121]
- Those who drink more than six cups of green tea a day cut can their risk for heart disease by a third. [122]



- Three cups of hibiscus tea a day for six weeks reduced systolic blood pressure by 7 mm Hg. [123]
- This is just as effective as Captopril, an ACE inhibitor commonly used to treat high blood pressure.

Alcohol

Moderate Alcohol Consumption: Good for your heart but with a price tag attached prevents heart disease but significantly increases risk of 7 different types of cancer.

Definitions:

- **Moderate alcohol consumption:** males up to 2 drinks a day, females 1 drink per day
- Binge drinking > 5 drinks per occasion.



- One drink is be defined as 12 oz of beer, 5 oz of wine, 8-9 oz of malt liquor or 1.5 oz of hard alcohol.
- A 2015 study including 115,000 adults from 12 countries. This study concluded that alcohol can reduce the risk of heart attack by 21 percent, but can increase cancer risk by 51 percent. This risk of cancer was increased by 20 percent for beer, 38 percent for wine, and 69 percent for spirits. [124]
- Alcohol consumption can cause oropharynx, larynx, esophagus, liver, colon, rectum, and female breast cancer
- Alcohol- attributed cancers make up 5.8 percent of cancer deaths. [125]
- Light/Moderate Drinking: In a study of more than 245,000 people, light/moderate drinking was associated with lower rate of cardiovascular death than completely abstaining. [126]
- Individuals who have never drank alcohol and are heavy drinkers are at higher risks for cardiovascular diseases compared to moderate drinking.
- A prospective study of 5,500 men and women showed that light to moderate drinking can decrease the risk of depression development by almost half compared to abstainers. Keep in mind that excessive alcohol use leads to depression! [127]
- In a recent observational cohort study of 550 men and women (none alcohol dependent) with weekly alcohol intake and cognitive performance measured repeatedly over 30 years demonstrated using MRI of the brain that even moderate drinking is associated with pathologic findings in the brain, including hippocampal atrophy (where memory is stored), vs. no drinking, In this study, researchers found that moderate drinking, within US safe limits, was associated with multiple adverse structural brain outcomes and faster cognitive decline, rather than being protective. There was no protective effect of mild drinking (defined as 1-7 drinks per week) versus abstinence. [128]
- Heavy drinking can cause cardiac arrhythmias including sinus tachycardia, sinus arrhythmia, premature atrial/ventricular complexes, atrial fibrillation/flutter. The normal prevalence of this rhythm issue is 1-4 percent but prevalence of arrhythmias is heavy drinkers at Munich Oktoberfest was 30.5 percent. Sinus tachycardia was the most prevalent arrhythmia that occurred. [129]
- In some patients even modest amount of alcohol can trigger atrial fibrillation!

So should I or should I not drink alcohol?

If you don't drink, do not start now, if you do, occasional beer or glass wine is ok. Given evidence that daily alcohol use even in moderation increases risk of cancer and cognitive impairment makes it difficult to recommend using it to prevent heart disease (dying of heart attack is definitely much more merciful than dying of cancer or dementia).

Humans are not the only creatures who get drunk!

- Bees can get drunk off of fermented pollen and sometimes can't find their way home or have flying incidents. Drunken bees that do find their way home to the hive after flying drunk are often punished and even attacked!
- Bohemian waxwing birds get drunk off fermented berries off of Rowan trees. Some of these birds don't know when to stop and crash from flying drunk! Some of the birds became so drunk they had to be admitted to rehab at the wildlife preserve in Yukon, Canada!



More info can be found at: [130] (https://www.buzzfeed.com/natashaumer/9-animals-that-could-teach-us-something-about-drugs-and-alco)



Vitamins

Vitamin sales are in the billions every year. [131]

- A study of over 160,000 women shows multivitamins has no influence on risk of common cancers or heart disease. [132]
- A study of over 13,000 males showed that regardless of nutrition status, multivitamin use did not reduce cardiovascular events. [133]
- Vitamins E and C show no effect in reducing heart attacks or stroke.



- Vitamin E: Doses over 400 IU/day can increase the risk of death. In a study of over 135,000 participants, nine of 11 trials with doses of over 400 IU/day showed an increased risk of mortality. Doses lower than 400 showed no effect. [134]
- High-dose folic acid and vitamins B-6 and B-12 do not reduce heart attack and stroke occurrence in high-risk populations. [135]
- Vitamin B6 and B12 drastically increased risk of lung cancer.

New research suggests long-term, high-dose supplementation with vitamins B6 and B12 -- long touted by the vitamin industry for increasing energy and improving metabolism, is associated with a two- to four-fold increased lung cancer risk in men relative to non-users. Risk was further elevated in male smokers taking more than 20 mg of B6 or 55 micrograms of B12 a day for 10 years. Male smokers taking B6 at this dose were three times more likely to develop lung cancer. Male smokers taking B12 at such doses were approximately four times more likely to develop the disease compared to non-users.

In addition, the B_6 and B_{12} associations were apparent in all histologic types except adenocarcinoma, which is the type less related to smoking. [136]

Calcium Supplements and Cardiovascular Events

• A 2016 study looking at over 2,700 participants showed that although dietary calcium intake helps to prevent heart disease while calcium supplement intake actually increases the risk. The study showed that supplement users had a 22 percent higher risk of the coronary calcium scores rising which caused atherosclerosis. Participants who had the highest dietary calcium intake did not have an increased risk for heart disease. [137]



- In a 2011 study of nearly 30,000 subjects, the use of calcium or calcium plus Vitamin D significantly increased both the risk of heart attack and the combined risk of heart attack and stroke.
- Calcium increased heart attack risk 25-30 percent and stroke risk 15-20 percent.
- In 1,000 people taking calcium (with or without Vitamin D six additional heart attacks or strokes would occur. This means that out of 178 taking calcium, one patient who would have otherwise been unharmed will have a stroke or heart attack. [138]

- Get your calcium from diet rather than supplements!
- Calcium supplements in women with cerebrovascular disease is associated with significant increase in risk of dementia!
- In a study published in October 2016 calcium supplementation was associated with 6.7-fold increased development of dementia in women with a history of stroke and a 3-fold increased risk of dementia with the presence of white matter lesions (known as small vessel disease), but not in groups without these conditions. [139]

Vitamin D

- Low vitamin D is a marker of risk for heart disease but probably not direct cause of it as such replacing it may not change that risk.
- A study also shows that taking high doses of Vitamin D once every month won't lower your risk of heart disease. This study only rules out monthly dosing. [140]



Fish Oil Supplements

- Fish oil supplements contain omega-3 fatty acids.
- These supplements provide no role in primary prevention of heart disease (without prior heart attack).



- A study shows that after a heart attack, high dose fish oil supplements may improve heart function and reduce scarring in undamaged muscle and markers if inflammation.
- Receiving fish oil every day for six months following a heart attack can reduce myocardial fibrosis by 5.6 percent and markers of inflammation by about 8 percent. [141]

Choose fish rather than fish oil!

Traditional Chinese medicine may benefit some CVD patients. Certain Chinese medications showed suggested benefits for each of the cardiovascular health conditions studied such as diabetes, high cholesterol and hypertension. For example, researchers looked at eight randomized controlled trials on traditional Chinese medicine and hypertension.

Tiankuijiangya, Zhongfujiangya, Qiqilian, Jiangya and Jiangyabao have antihypertensive effects and a good safety profile, making them a potential good alternative for patients intolerant of or who cannot afford Western medications.

Medications such as the Jiangzhitongluo capsule, Salvia miltiorrhiza and Pueraria lobata capsule, and Zhibitai capsule have a potent lipid-lowing effect, but there are no studies to see if those effects would reduce cardiovascular events



Medications such as Xiaoke, Tangminling, Jinlida, and Jianyutangkang have a potent effect on blood sugar control and beta cell function (cells in the pancreas producing insulin) in those with type 2 diabetes.

Medications, such as Tangzhiping and Tianqi, may possibly prevent the progression of prediabetes to diabetes; however, the effects on long-term outcomes are unknown.

Treatment with certain traditional Chinese medications might be effective in alleviating angina or neurological deficits in patients with coronary artery disease or ischemic stroke, while Xuezhikang might reduce cardiovascular events after myocardial infarction; however, large scale studies are needed before definite conclusions can be drawn. [142]



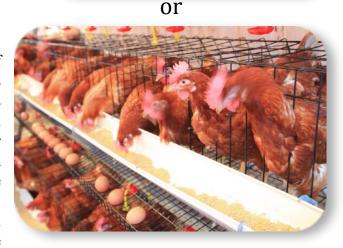
Organic versus not organic:





Published facts:

Organic crops have higher antioxidant activity and between 18 and 69 percent higher concentrations of a range of individual antioxidants; increased intakes of polyphenolics and antioxidants has been linked to a reduced risk of certain chronic diseases such as cardiovascular and neurodegenerative diseases and certain cancers. Conventional crops have higher levels of the toxic metal cadmium, and are four-times more likely to contain detectable pesticide residues; there are



general recommendations to minimize the intake of pesticides and cadmium to avoid potential negative health impacts. [143]

Organic meat, milk, and dairy products have approximately 50 percent higher concentrations of nutritionally-desirable omega-3 fatty acids. [143], [144]

There is virtually no published data from long-term studies focusing on chronic diseases (such as cardiovascular disease, diabetes, cancer, and neurodegenerative conditions) and controlled human dietary intervention studies comparing effects of organic and conventional diets. It is therefore currently not possible to quantify to what extent organic food consumption may affect human health. [145]

To check financial impact on your grocery budget when changing from conventional to organic go to:

(http://www.businessinsider.com/cost-comparison-of-organic-and-regular-food-2015-8/#almond-butter-222220)





Benefits of Cooked Vegetables

Cooking vegetables can make the cell walls less rigid, which makes it easier to absorb certain nutrients and digest food better. Compared to raw carrots, cooked carrots, for example, have more beta carotene, an antioxidant that can be converted to vitamin A and improves bone, eye, and reproductive health. The amount of lycopene, a carotenoid that has been associated with reduced incidence of heart disease and cancer, increases when tomatoes are cooked. Other vegetables which release more ingredients are asparagus, spinach, mushrooms.

Benefits of Raw Vegetables

Boiling and cooking vegetables in high temperatures or in water decreases their nutrient levels. Water-soluble vitamins such as vitamin C and B vitamins are often lost during these cooking processes. Minerals like potassium, phosphorus, calcium, magnesium, iron and zinc may be reduced by up to 60 to 70 percent. Glucosinolate in broccoli that may help fight cancer decreased when the vegetable is boiled. Beets when cooked lose 25 percent of folic acid (but nitrates are not affected), garlic cooking decreases phytonutrient allicin, which is responsible for lipid-lowering, anti-blood coagulation, anti-hypertension, anti-cancer, antioxidant and anti-microbial effects. Red peppers: lose vitamin C when roasted or grilled above 375 F. The amount of nutrients lost during cooking depends on many factors including preparation cooking methods and duration of cooking.

Modified from:

(http://healthyeating.sfgate.com/raw-vegetables-vs-cooked-vegetables-5344.html)

Verdict

Eat your vegetables anyway you like them!

References:

- 1. Gibbons, A., The Evolution of Diet. National Graphic Magazine, 2017.
- 2. Vegan, W., Refined Sugar History. Whole Vegan Inc, 2017.
- 3. Magness, S., *The Genetics of Obesity: The Thrifty Gene Hypothesis*. The Science of Running, 2010.
- 4. Iqbal, R., et al., *Dietary patterns and the risk of acute myocardial infarction in 52 countries: results of the INTERHEART study.* Circulation, 2008. **118**(19): p. 1929-37.
- 5. Shikany, J.M., et al., Southern Dietary Pattern is Associated With Hazard of Acute Coronary Heart Disease in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. Circulation, 2015. **132**(9): p. 804-14.
- 6. Li, F., et al., Associations of dietary patterns with the risk of all-cause, CVD and stroke mortality: a meta-analysis of prospective cohort studies. Br J Nutr, 2015. 113(1): p. 16-24.
- 7. Veronese, N., et al., *Fried potato consumption is associated with elevated mortality: an 8-y longitudinal cohort study.* Am J Clin Nutr, 2017. **106**(1): p. 162-167.
- 8. Daniel, C.R., et al., *Trends in meat consumption in the United States*. Public Health Nutr, 2011. **14**(4): p. 575-83.
- 9. O'Connell, T.C., et al., *The diet-body offset in human nitrogen isotopic values: a controlled dietary study.* Am J Phys Anthropol, 2012. **149**(3): p. 426-34.
- 10. Kaluza, J., A. Akesson, and A. Wolk, *Processed and unprocessed red meat consumption and risk of heart failure: prospective study of men.* Circ Heart Fail, 2014. 7(4): p. 552-7.
- 11. Micha, R., S.K. Wallace, and D. Mozaffarian, *Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes: A systematic review and meta-analysis.* Circulation, 2010. **121**(21): p. 2271-83.
- 12. Tang, W.W., et al., *Intestinal Microbial Metabolism of Phosphatidylcholine and Cardiovascular Risk.* N Engl J Med, 2013. **368**(17): p. 1575-84.
- 13. Etemadi, A., et al., Mortality from different causes associated with meat, heme iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study: population based cohort study. Bmj, 2017. **357**: p. j1957.
- 14. Lowette, K., et al., *Effects of high-fructose diets on central appetite signaling and cognitive function.* Front Nutr, 2015. **2**: p. 5.
- 15. Malik, V.S., et al., Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care, 2010. **33**(11): p. 2477-83.
- 16. Yang, Q., et al., *Added sugar intake and cardiovascular diseases mortality among US adults.* JAMA Intern Med, 2014. **174**(4): p. 516-24.
- 17. Association, A.H., *Added Sugars Add to Your Risk of Dying from Heart Disease*. American Heart Association, 2017. **Healthy Living**.
- 18. Azad, M.B., et al., Association Between Artificially Sweetened Beverage Consumption During Pregnancy and Infant Body Mass Index. JAMA Pediatr, 2016. **170**(7): p. 662-70.
- 19. Azad, M.B., et al., *Nonnutritive sweeteners and cardiometabolic health: a systematic review and meta-analysis of randomized controlled trials and prospective cohort studies.* Cmaj, 2017. **189**(28): p. E929-e939.

- 20. Pase, M.P., et al., Sugar- and Artificially Sweetened Beverages and the Risks of Incident Stroke and Dementia: A Prospective Cohort Study. Stroke, 2017. **48**(5): p. 1139-1146.
- 21. O'Keefe, J.H., N.M. Gheewala, and J.O. O'Keefe, *Dietary strategies for improving post-prandial glucose, lipids, inflammation, and cardiovascular health.* J Am Coll Cardiol, 2008. **51**(3): p. 249-55.
- 22. Odegaard, A.O., et al., Western-style fast food intake and cardiometabolic risk in an Eastern country. Circulation, 2012. **126**(2): p. 182-8.
- 23. Ruberg, F.L., *Paying at the pump: diet-induced accumulation of cardiac lipid and systolic dysfunction*, in *Circ Cardiovasc Imaging*. 2010: United States. p. 635-7.
- 24. Jahren, A.H. and R.A. Kraft, *Carbon and nitrogen stable isotopes in fast food: signatures of corn and confinement.* Proc Natl Acad Sci U S A, 2008. **105**(46): p. 17855-60.
- 25. Estruch, R., et al., *Primary prevention of cardiovascular disease with a Mediterranean diet.* N Engl J Med, 2013. **368**(14): p. 1279-90.
- 26. Esposito, K., et al., *Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial.* Ann Intern Med, 2009. **151**(5): p. 306-14.
- 27. Salas-Salvado, J., et al., *Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial.* Diabetes Care, 2011. **34**(1): p. 14-9.
- 28. Toledo, E., et al., *Mediterranean Diet and Invasive Breast Cancer Risk Among Women at High Cardiovascular Risk in the PREDIMED Trial: A Randomized Clinical Trial.* JAMA Intern Med, 2015. **175**(11): p. 1752-60.
- 29. Hernaez, A., et al., *Mediterranean Diet Improves High-Density Lipoprotein Function in High-Cardiovascular-Risk Individuals: A Randomized Controlled Trial.* Circulation, 2017. **135**(7): p. 633-643.
- 30. Hogg, R.E., et al., *Mediterranean Diet Score and Its Association with Age-Related Macular Degeneration: The European Eye Study.* Ophthalmology, 2017. **124**(1): p. 82-89.
- 31. Cachulo Mda, L., et al., *Prevalence of Age-Related Macular Degeneration in Portugal: The Coimbra Eye Study Report 1*. Ophthalmologica, 2015. **233**(3-4): p. 119-27.
- 32. Haring, B., et al., *Dietary Patterns and Fractures in Postmenopausal Women: Results From the Women's Health Initiative*. JAMA Intern Med, 2016. **176**(5): p. 645-52.
- 33. Luciano, M., et al., *Mediterranean-type diet and brain structural change from 73 to 76 years in a Scottish cohort.* Neurology, 2017. **88**(5): p. 449-455.
- 34. Crous-Bou, M., et al., *Mediterranean diet and telomere length in Nurses' Health Study:* population based cohort study. Bmj, 2014. **349**: p. g6674.
- 35. Gallego RM, U.I., Moreno-Franco B et al., Adherence to a Mediterranean diet is associated with the presence and extent of asymptomatic adults: The AWHS study., in European Atherosclerosis Society Annual Congress. 2017: Prague, Czech Republic.
- 36. Tuso, P.J., et al., *Nutritional Update for Physicians: Plant-Based Diets*, in *Perm J.* 2013. p. 61-6.
- 37. Wright, N., et al., *The BROAD study: A randomised controlled trial using a whole food plant-based diet in the community for obesity, ischaemic heart disease or diabetes.* Nutrition & Diabetes, 2017. **7**(3).

- 38. Satija, A., et al., *Healthful and Unhealthful Plant-Based Diets and the Risk of Coronary Heart Disease in U.S. Adults.* J Am Coll Cardiol, 2017. **70**(4): p. 411-422.
- 39. Imai, E., et al., *Animal protein intake is associated with higher-level functional capacity in elderly adults: the Ohasama study.* J Am Geriatr Soc, 2014. **62**(3): p. 426-34.
- 40. He, F.J. and G.A. MacGregor, *A comprehensive review on salt and health and current experience of worldwide salt reduction programmes*. J Hum Hypertens, 2009. **23**(6): p. 363-84.
- 41. Mente, A., et al., Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies. Lancet, 2016. **388**(10043): p. 465-75.
- 42. Harnack, L.J., et al., *Sources of Sodium in US Adults From 3 Geographic Regions*. Circulation, 2017. **135**(19): p. 1775-1783.
- 43. Press, N.A., Front Matter | Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate | The National Academies Press. 2005, Food and Nutrition Board Instit of Medicine.
- 44. van Mierlo, L.A., et al., *Suboptimal potassium intake and potential impact on population blood pressure*. Arch Intern Med, 2010. **170**(16): p. 1501-2.
- 45. D'Elia, L., et al., *Potassium intake, stroke, and cardiovascular disease a meta-analysis of prospective studies.* J Am Coll Cardiol, 2011. **57**(10): p. 1210-9.
- 46. Hughes, S., *AHA Issues 'Presidential Advisory' on Harms of Saturated Fat.* Medscape Medical News, 2017.
- 47. de Oliveira Otto, M.C., et al., *Dietary intake of saturated fat by food source and incident cardiovascular disease: the Multi-Ethnic Study of Atherosclerosis.* Am J Clin Nutr, 2012. **96**(2): p. 397-404.
- 48. Yakoob, M.Y., et al., Circulating Biomarkers of Dairy Fat and Risk of Incident Diabetes Mellitus Among US Men and Women in Two Large Prospective Cohorts. Circulation, 2016.
- 49. Pimpin, L., et al., *Is Butter Back? A Systematic Review and Meta-Analysis of Butter Consumption and Risk of Cardiovascular Disease, Diabetes, and Total Mortality.* PLoS One, 2016. **11**(6): p. e0158118.
- 50. Sacks, F.M., et al., *Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association*. Circulation, 2017. **136**(3): p. e1-e23.
- 51. Dehghan, M., et al., Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet, 2017.
- 52. Brandt, E.J., et al., *Hospital Admissions for Myocardial Infarction and Stroke Before and After the Trans-Fatty Acid Restrictions in New York.* JAMA Cardiol, 2017. **2**(6): p. 627-634.
- 53. Mozaffarian, D., et al., *Trans fatty acids and cardiovascular disease*. N Engl J Med, 2006. **354**(15): p. 1601-13.
- 54. Bowman, G.L., et al., *Nutrient biomarker patterns, cognitive function, and MRI measures of brain aging.* Neurology, 2012. **78**(4): p. 241-9.
- 55. health.gov. 2015 Dietary Guidelines Advisory Committee Membership health.gov. 2015; Available from: https://health.gov/dietaryguidelines/2015-scientific-report/01-DGAC-staff-membership.asp.

- 56. Kratz, M., *Dietary cholesterol, atherosclerosis and coronary heart disease*. Handb Exp Pharmacol, 2005(170): p. 195-213.
- 57. Hu, F.B., et al., A prospective study of egg consumption and risk of cardiovascular disease in men and women. Jama, 1999. **281**(15): p. 1387-94.
- 58. Diez-Espino, J., et al., *Egg consumption and cardiovascular disease according to diabetic status: The PREDIMED study.* Clin Nutr, 2017. **36**(4): p. 1015-1021.
- 59. Park, Y., et al., *Dietary fiber intake and mortality in the NIH-AARP diet and health study.* Arch Intern Med, 2011. **171**(12): p. 1061-8.
- 60. Bazzano, L.A., et al., *Intake of fruit, vegetables, and fruit juices and risk of diabetes in women.* Diabetes Care, 2008. **31**(7): p. 1311-7.
- 61. Guasch-Ferre, M., et al., *Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study.* BMC Med, 2014. **12**: p. 78.
- 62. Sanchez-Villegas, A., et al., *Dietary fat intake and the risk of depression: the SUN Project.* PLoS One, 2011. **6**(1): p. e16268.
- 63. Pitt, J., et al., *Alzheimer's-associated Abeta oligomers show altered structure, immunoreactivity and synaptotoxicity with low doses of oleocanthal.* Toxicol Appl Pharmacol, 2009. **240**(2): p. 189-97.
- 64. Garcia-Martinez, O., et al., *The effect of olive oil on osteoporosis prevention*. Int J Food Sci Nutr, 2014. **65**(7): p. 834-40.
- 65. Scotece, M., et al., New drugs from ancient natural foods. Oleocanthal, the natural occurring spicy compound of olive oil: a brief history. Drug Discov Today, 2015. **20**(4): p. 406-10.
- 66. Cassidy, A., et al., *Habitual intake of flavonoid subclasses and incident hypertension in adults*. Am J Clin Nutr, 2011. **93**(2): p. 338-47.
- 67. Cassidy, A., et al., *High anthocyanin intake is associated with a reduced risk of myocardial infarction in young and middle-aged women.* Circulation, 2013. **127**(2): p. 188-96.
- 68. Devore, E.E., et al., *Dietary intakes of berries and flavonoids in relation to cognitive decline*. Ann Neurol, 2012. **72**(1): p. 135-43.
- 69. Aune, D., et al., Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. Int J Epidemiol, 2017.
- 70. Wang, L., et al., Effect of a moderate fat diet with and without avocados on lipoprotein particle number, size and subclasses in overweight and obese adults: a randomized, controlled trial. J Am Heart Assoc, 2015. 4(1): p. e001355.
- 71. Zampelas, A., et al., Fish consumption among healthy adults is associated with decreased levels of inflammatory markers related to cardiovascular disease: the ATTICA study. J Am Coll Cardiol, 2005. **46**(1): p. 120-4.
- 72. Studer, M., et al., *Effect of different antilipidemic agents and diets on mortality: a systematic review.* Arch Intern Med, 2005. **165**(7): p. 725-30.
- 73. Mozaffarian, D., et al., *Fish intake and risk of incident atrial fibrillation*. Circulation, 2004. **110**(4): p. 368-73.
- 74. Morris, M.C., et al., Association of Seafood Consumption, Brain Mercury Level, and APOE epsilon4 Status With Brain Neuropathology in Older Adults. Jama, 2016. **315**(5): p. 489-97.

- 75. Tedeschi, S.K., et al., *The relationship between fish consumption and disease activity in rheumatoid arthritis*. Arthritis Care Res (Hoboken), 2017.
- 76. Stephen, N.M., et al., *Effect of different types of heat processing on chemical changes in tuna*. J Food Sci Technol, 2010. **47**(2): p. 174-81.
- 77. Nahab, F., et al., *Dietary fried fish intake increases risk of CVD: the REasons for Geographic And Racial Differences in Stroke (REGARDS) study.* Public Health Nutr, 2016. **19**(18): p. 3327-3336.
- 78. Mozaffarian, D., et al., *Mercury Exposure and Risk of Cardiovascular Disease in Two U.S. Cohorts.* N Engl J Med, 2011. **364**(12): p. 1116-25.
- 79. Greenfield, N., The Smart Seafood Buying Guide. NRDC, 2015.
- 80. Weaver, K.L., et al., *The content of favorable and unfavorable polyunsaturated fatty acids found in commonly eaten fish.* J Am Diet Assoc, 2008. **108**(7): p. 1178-85.
- 81. Harris, W.S., et al., Omega-6 fatty acids and risk for cardiovascular disease: a science advisory from the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. Circulation, 2009. 119(6): p. 902-7.
- 82. Rodriguez-Leyva, D., et al., *The cardiovascular effects of flaxseed and its omega-3 fatty acid, alpha-linolenic acid.* Can J Cardiol, 2010. **26**(9): p. 489-96.
- 83. Schor, J., Flaxseed Reduces High Blood Pressure. Natural Medicine Journal, 2014. 6(3).
- 84. Buijsse, B., et al., *Chocolate consumption in relation to blood pressure and risk of cardiovascular disease in German adults.* Eur Heart J, 2010. **31**(13): p. 1616-23.
- 85. Grassi, D., et al., *Short-term administration of dark chocolate is followed by a significant increase in insulin sensitivity and a decrease in blood pressure in healthy persons.* Am J Clin Nutr, 2005. **81**(3): p. 611-4.
- 86. Mostofsky, E., et al., *Chocolate intake and incidence of heart failure: a population-based prospective study of middle-aged and elderly women.* Circ Heart Fail, 2010. **3**(5): p. 612-6.
- 87. Buijsse, B., et al., *Cocoa intake, blood pressure, and cardiovascular mortality: the Zutphen Elderly Study.* Arch Intern Med, 2006. **166**(4): p. 411-7.
- 88. Heiss, C., et al., *Acute consumption of flavanol-rich cocoa and the reversal of endothelial dysfunction in smokers.* J Am Coll Cardiol, 2005. **46**(7): p. 1276-83.
- 89. Grassi, D., et al., Cocoa reduces blood pressure and insulin resistance and improves endothelium-dependent vasodilation in hypertensives. Hypertension, 2005. **46**(2): p. 398-405.
- 90. Loffredo, L., et al., *Dark chocolate acutely improves walking autonomy in patients with peripheral artery disease.* J Am Heart Assoc, 2014. **3**(4).
- 91. Crichton, G.E., M.F. Elias, and A. Alkerwi, *Chocolate intake is associated with better cognitive function: The Maine-Syracuse Longitudinal Study.* Appetite, 2016. **100**: p. 126-32.
- 92. Greenberg, J.A., Chocolate intake and diabetes risk. Clin Nutr, 2015. 34(1): p. 129-33.
- 93. Golomb, B.A., S. Koperski, and H.L. White, *Association between more frequent chocolate consumption and lower body mass index*. Arch Intern Med, 2012. **172**(6): p. 519-21.
- 94. Sabate, J., K. Oda, and E. Ros, *Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials.* Arch Intern Med, 2010. **170**(9): p. 821-7.
- 95. Ros, E., Health Benefits of Nut Consumption. Nutrients, 2010. 2(7): p. 652-82.

- 96. Aune, D., et al., Nut consumption and risk of cardiovascular disease, total cancer, all-cause and cause-specific mortality: a systematic review and dose-response meta-analysis of prospective studies. BMC Med, 2016. **14**(1): p. 207.
- 97. Frazier, A.L., et al., *Prospective study of peripregnancy consumption of peanuts or tree nuts by mothers and the risk of peanut or tree nut allergy in their offspring*. JAMA Pediatr, 2014. **168**(2): p. 156-62.
- 98. Farr, O.M., et al., Walnut consumption increases activation of the insula to highly desirable food cues: A randomized, double-blind, placebo-controlled, cross-over fMRI study. Diabetes Obes Metab, 2017.
- 99. Djousse, L. and J.M. Gaziano, *Breakfast cereals and risk of heart failure in the physicians' health study I.* Arch Intern Med, 2007. **167**(19): p. 2080-5.
- 100. Moreyra, A.E., A.C. Wilson, and A. Koraym, *Effect of combining psyllium fiber with simvastatin in lowering cholesterol*. Arch Intern Med, 2005. **165**(10): p. 1161-6.
- 101. Block, G., et al., Vitamin C in plasma is inversely related to blood pressure and change in blood pressure during the previous year in young Black and White women. Nutr J, 2008. 7: p. 35.
- 102. Jonsson, C. and L. Ellegård, *Grapefruit juice and serum lipids in healthy adults*. Scandinavian Journal of Food and Nutrition, 2006. **50**(3).
- 103. Gorinstein, S., et al., Red grapefruit positively influences serum triglyceride level in patients suffering from coronary atherosclerosis: studies in vitro and in humans. J Agric Food Chem, 2006. **54**(5): p. 1887-92.
- 104. Cao, H., et al., *Insulin and cinnamon polyphenols increase the amount of insulin receptor b, glucose transporter 4, and anti-inflammatory protein tristetraprolin in mouse 3T3-L1 adipocytes.* The FASEB Journal, 2006. **20**(A939).
- 105. Lebwohl, B., et al., Long term gluten consumption in adults without celiac disease and risk of coronary heart disease: prospective cohort study. Bmj, 2017. **357**: p. j1892.
- 106. Prevention, C.f.D.C.a., *Healthy Water/Drinking Index*. Center for Disease Control and Prevention, 2015.
- 107. Zelman, K.M., The Wonders of Water. WebMD, 2017.
- 108. Valtin, H. "Drink at Least 8 Glasses of Water a Day" Really? 2002; Available from: http://www.dartmouth.edu/~news/releases/2002/aug/080802.html.
- 109. Alexander, D.D., et al., *Dairy consumption and CVD: a systematic review and meta-analysis.* Br J Nutr, 2016. **115**(4): p. 737-50.
- 110. Mozaffarian, D., et al., *Trans-palmitoleic acid, metabolic risk factors, and new-onset diabetes in U.S. adults: a cohort study.* Ann Intern Med, 2010. **153**(12): p. 790-9.
- 111. Kempf, K., et al., *Effects of coffee consumption on subclinical inflammation and other risk factors for type 2 diabetes: a clinical trial.* Am J Clin Nutr, 2010. **91**(4): p. 950-7.
- 112. Bhupathiraju, S.N., et al., *Changes in coffee intake and subsequent risk of type 2 diabetes:* three large cohorts of US men and women. Diabetologia, 2014. **57**(7): p. 1346-54.
- 113. Cheng, M., et al., *Caffeine intake and atrial fibrillation incidence: dose response meta-analysis of prospective cohort studies*. Can J Cardiol, 2014. **30**(4): p. 448-54.
- 114. Dixit, S., Consumption of "Healthy" Caffeinated Products and Cardiac Ectopy, in Heart Rhythm Society. 2015: Boston, MA.

- 115. Kapil, V., et al., *Dietary nitrate provides sustained blood pressure lowering in hypertensive patients: a randomized, phase 2, double-blind, placebo-controlled study.* Hypertension, 2015. **65**(2): p. 320-7.
- 116. Webb, A.J., et al., *Acute blood pressure lowering, vasoprotective, and antiplatelet properties of dietary nitrate via bioconversion to nitrite.* Hypertension, 2008. **51**(3): p. 784-90.
- 117. Coggan, A.R., et al., *Acute Dietary Nitrate Intake Improves Muscle Contractile Function in Patients With Heart Failure: A Double-Blind, Placebo-Controlled, Randomized Trial.* Circ Heart Fail, 2015. **8**(5): p. 914-20.
- 118. Sumner, M.D., et al., *Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease.* Am J Cardiol, 2005. **96**(6): p. 810-4.
- 119. Ruel, G., *A cup of cranberry juice a day increasesHDL cholesterol.*, in *Canadian Cardiovascular Congress*. 2004: Calgary, Alberta, Canada.
- 120. Miller, P.E., et al., Associations of Coffee, Tea, and Caffeine Intake with Coronary Artery Calcification and Cardiovascular Events. Am J Med, 2017. **130**(2): p. 188-197.e5.
- 121. Maron, D.J., et al., *Cholesterol-lowering effect of a theaflavin-enriched green tea extract: a randomized controlled trial.* Arch Intern Med, 2003. **163**(12): p. 1448-53.
- 122. Mason, E., Tea and coffee 'protect hearts'. BBC News News, 2010.
- 123. Whelton, P.K., et al., *Primary prevention of hypertension: clinical and public health advisory from The National High Blood Pressure Education Program.* Jama, 2002. **288**(15): p. 1882-8.
- 124. Smyth, A., et al., *Alcohol consumption and cardiovascular disease, cancer, injury, admission to hospital, and mortality: a prospective cohort study.* Lancet, 2015. **386**(10007): p. 1945-54.
- 125. Connor, J., Alcohol consumption as a cause of cancer. Addiction, 2017. 112(2): p. 222-228.
- 126. Mukamal, K.J., et al., *Alcohol consumption and cardiovascular mortality among U.S. adults*, 1987 to 2002. J Am Coll Cardiol, 2010. **55**(13): p. 1328-35.
- 127. Gea, A., et al., *Alcohol intake, wine consumption and the development of depression: the PREDIMED study.* BMC Med, 2013. **11**: p. 192.
- 128. Topiwala, A., et al., *Moderate alcohol consumption as risk factor for adverse brain outcomes and cognitive decline: longitudinal cohort study.* Bmj, 2017. **357**: p. j2353.
- 129. Brunner, S., et al., Alcohol consumption, sinus tachycardia, and cardiac arrhythmias at the Munich Octoberfest: results from the Munich Beer Related Electrocardiogram Workup Study (MunichBREW). Eur Heart J, 2017.
- 130. Umer, N., 9 Animals That Get Drunk Or High. BuzzFeed, 2014.
- 131. Sesso, H.D., et al., Vitamins E and C in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. Jama, 2008. **300**(18): p. 2123-33.
- 132. Neuhouser, M.L., et al., *Multivitamin use and risk of cancer and cardiovascular disease in the Women's Health Initiative cohorts.* Arch Intern Med, 2009. **169**(3): p. 294-304.
- 133. Rautiainen, S., et al., Effect of Baseline Nutritional Status on Long-term Multivitamin Use and Cardiovascular Disease Risk: A Secondary Analysis of the Physicians' Health Study II Randomized Clinical Trial. JAMA Cardiol, 2017. 2(6): p. 617-625.
- 134. Miller, E.R., 3rd, et al., *Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality.* Ann Intern Med, 2005. **142**(1): p. 37-46.

- 135. Lonn, E., et al., *Homocysteine lowering with folic acid and B vitamins in vascular disease.* N Engl J Med, 2006. **354**(15): p. 1567-77.
- 136. Brasky, T.M., E. White, and C.L. Chen, Long-Term, Supplemental, One-Carbon Metabolism-Related Vitamin B Use in Relation to Lung Cancer Risk in the Vitamins and Lifestyle (VITAL) Cohort. J Clin Oncol, 2017: p. Jco2017727735.
- 137. Medicine, J.H. *Calcium Supplements May Damage the Heart 10/11/2016*. Johns Hopkins Medicine News and Publications, 2016.
- 138. Bolland, M.J., et al., Calcium supplements with or without vitamin D and risk of cardiovascular events: reanalysis of the Women's Health Initiative limited access dataset and meta-analysis. Bmj, 2011. **342**: p. d2040.
- 139. Kern, J., et al., Calcium supplementation and risk of dementia in women with cerebrovascular disease. Neurology, 2016. **87**(16): p. 1674-1680.
- 140. Scragg, R., et al., Effect of Monthly High-Dose Vitamin D Supplementation on Cardiovascular Disease in the Vitamin D Assessment Study: A Randomized Clinical Trial. JAMA Cardiol, 2017. **2**(6): p. 608-616.
- 141. Siscovick, D.S., et al., Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation and the Prevention of Clinical Cardiovascular Disease: A Science Advisory From the American Heart Association. Circulation, 2017. 135(15): p. e867-e884.
- 142. Hao, P., et al., *Traditional Chinese Medicine for Cardiovascular Disease: Evidence and Potential Mechanisms*. J Am Coll Cardiol, 2017. **69**(24): p. 2952-2966.
- 143. Średnicka-Tober, D., et al., *Composition differences between organic and conventional meat: a systematic literature review and meta-analysis.* Br J Nutr, 2016. **115**(6): p. 994-1011.
- 144. Średnicka-Tober, D., et al., *Higher PUFA and n-3 PUFA, conjugated linoleic acid, α-tocopherol and iron, but lower iodine and selenium concentrations in organic milk: a systematic literature review and meta- and redundancy analyses.* Br J Nutr, 2016. **115**(6): p. 1043-60.
- 145. Barański, M., et al., *Effects of organic food consumption on human health; the jury is still out!* Food Nutr Res, 2017. **61**(1).

In 1953, Morris and colleagues published a paper showing that mortality from coronary heart disease (CHD) was more than twice as high in sedentary London bus drivers compared with physically active conductors. This pioneering work gave rise to the hypothesis that physical activity might be of importance in prevention of heart disease. [1]

Types of Exercise:

(Adopted form National Institute on Aging at NIH) [2]

Endurance

Endurance, or aerobic, activities increase your breathing and heart rate. They keep your heart, lungs, and circulatory system healthy and improve your overall fitness. Building your endurance makes it easier to carry out many of your everyday activities.

- Brisk walking or jogging
- Yard work (mowing, raking, digging)
- Dancing



Strength (resistance)

Strength exercises make your muscles stronger. Even small increases in strength can make a big difference in your ability to stay independent and carry out everyday activities, such as climbing stairs and carrying groceries. These exercises also are called "strength training" or "resistance training."

- Lifting weights
- Using a resistance band
- Using your own body weight

Balance

Balance exercises help prevent falls, a common problem in older adults. Many lower-body strength exercises also will improve your balance.

- Standing on one foot
- Heel-to-toe walk
- Tai Chi



Flexibility

Flexibility exercises stretch your muscles and can help your body stay limber. Being flexible gives you more freedom of movement for other exercises as well as for your everyday activities.

- Shoulder and upper arm stretch
- Calf stretch
- Yoga

For more exercise ideas go to: (https://go4life.nia.nih.gov/mygo4life) [3]



Exercise Recommendations by Center for Disease Control and Prevention [4]

Adults

- Health benefits are gained for just doing a minimum of 60 minutes of exercise a week, but for major benefits more is recommended. Adults should preform moderate-intensity aerobic activity for at least 150 minutes a week or 75 minutes of vigorous aerobic activity.
- More exercise = greater benefits! You can increase your exercise amounts to moderateintensity aerobic activity for 300 minutes a week or 150 minutes of vigorous aerobic activity for increased benefits.
- One minute of vigorous activity is equivalent to 2 minutes of moderate exercise.
- Muscle strengthening activities such as lifting weights, working with resistance bands, doing setups and pushups, yoga, and heavy gardening should be done two or more times a week. Aerobic activity should be done throughout the week for at least ten minutes at a time.

Adults Aged 65 or Older

- Older adults should attempt to complete the same amount of exercise as adults. If this is not possible, try to be as active as possible. For individuals at risk of falling make sure you do exercises such as standing on one leg, walking backwards or sideways.
- Remember to slowly increase your exercise activity level if you are just starting out. Avoid vigorous activity at first and work up to it!
- Keep in mind that starting strenuous activity, if you have not done much exercise for long time, is associated with increased risk of heart attack. Consult your doctor before starting exercise program and if eligible consider joining cardiac rehab.

- Moderate-intensity aerobic activity means you're working hard enough to raise your heart rate and break a sweat. One way to tell is that you'll be able to talk, but not sing the words to your favorite song. Here are some examples of activities that require moderate effort:
 - Walking fast
 - Doing water aerobics
 - Riding a bike on level ground or with few hills
 - ▶ Playing doubles tennis
 - ▶ Pushing a lawn mower

Build Up Over Time

- If you want to do more vigorous-level activities, slowly replace those that take moderate effort like brisk walking, with more vigorous activities like jogging. Vigorous-intensity aerobic activity means you're breathing hard and fast, and your heart rate has gone up quite a bit. If you're working at this level, you won't be able to say more than a few words without pausing for a breath. Here are some examples of activities that require vigorous effort:
 - Jogging or running
 - Swimming laps
 - Riding a bike fast or on hills
 - Playing singles tennis
 - Playing basketball
- 10 minutes at a time is fine! We know 150 minutes each week sounds like a lot of time, but it's not. That's 2 hours and 30 minutes; about the same amount of time you might spend watching a movie. The good news is that you can spread



your activity out during the week, so you don't have to do it all at once.

What is the difference between activities of daily living and structured exercise?

- Activities of daily living (ADLs) are the activities you do on a regular basis that can help to burn calories, maintain strength and agility, and keep active. Examples of these include washing the car, gardening, raking leaves, washing dishes, vacuuming, etc. These activities do not necessarily count as exercise. Be sure to note the distinction in these ADLs as compared to structured exercises. You need both types of movement in order to maintain an optimal level of physical activity.
- Structured exercise includes activities specifically geared toward a purpose, usually to improve cardiovascular fitness, strength, flexibility, or balance and agility. There are specific definitions as to what constitutes exercise. Some activities may fit into both categories (exercise and ADLs) based on the intensity and duration. One example of an activity fitting both categories would be walking while mowing the lawn. [2]

Even very light activity decreased risk of death.

- Using accelerometers to precisely measure physical activity, researchers have found that even very light exercise, well below the generally recommended levels, reduces mortality in older women.
- The scientists had 6,382 women ages 63 to 99 wear an accelerometer for seven consecutive days, waking and sleeping, except when bathing or swimming. Using this data, they were able to precisely quantify levels of activity without having to rely on self-reports, which can be unreliable.
- For each 30 minute a day increase in moderate-to-vigorous physical activity, there was a 39 percent decrease in all-cause mortality. But they also found that 30 minutes of even very light activity, doing light household chores, walking slowly over short distances was tied to a 12 percent reduction in mortality.



The results apply to all women, all races, regardless of weight and even for women over 80. [5]

Weekend warriors

- A 2017 study published in JAMA with 63,591 participants found that although these are the recommendations, individuals not meeting guidelines (only 1 or 2 sessions a week) and "weekend warriors" (fit exercise recommendations into the 2 day weekend) also saw a decrease in all-cause, CVD and cancer mortality.
- These individuals along with regularly active participants saw a 30 percent reduced risk in allcause mortality compared to inactive individuals. [5]

Which sport is the best to prevent death (or rather delay it...)?

• A large study of over 80,000 participants demonstrated that reductions in all-cause and cardiovascular mortality might best be achieved by participating in sports including cycling, swimming, racquet sports (tennis, squash) and aerobics (defined as gymnastics, dancing) but surprisingly not with jogging and football! [6]

What about just walking?

• A 2017 study published in The International Journal of Obesity, observed 111 participants that ranged from being almost completely sedentary during the day to walking about 15,000 steps per day. The study included 55 office workers and 56 walking/delivery workers

(postal service workers). Results found that the postal workers walking an average of about 15,000 steps (about 7 miles) had no metabolic syndrome features and had the lowest coronary heart disease risk compared to the sedentary office workers. [7]

Whenever you can, hit the Great (or just any) Outdoors!

Long walks can improve moods and reduce anxiety, but the benefits may be greatest if the walks take place outdoors rather than in a gym according to researchers evaluating individuals exercising on treadmill versus hiking in the Austrian Alps. Mountain hiking resulted in significant improvement in mood and participants reported feeling less fatigued (despite quite strenuous hike) as compared to walking on treadmill. For those of us who do not have Alps in their backyards, a vigorous walk in the woods



near home will provide the mental boost we need to keep us going.

Sitting, the new smoking....

- A 2015 analysis concluded that prolonged sitting is associated with higher mortality rates from cancer, diabetes, and cardiovascular disease. This is regardless of activity level! (exercise did not correct this association) Remember the healthiest population of humans, the Tsimane, (see chapter 1) spend less than 10 percent of their wake time sitting! [8]
- Women who do less physical activities than 40 minutes a day had shorter telomeres (caps on our chromosomes that protect them and determine life expectancy) by 170 base pairs. [8]
- Prolonged sitting is associated with nonalcoholic fatty liver disease (NAFLD) according to a study conducted from 2011-2013 with 139,000 participants. The study, published in The Journal of Hepatology, found the increased prevalence for NAFLD with more than 5 hours of sitting a day. [9]



Sedentary Time Ups CVD Risk in Dose-Response Way

• Pandey and colleagues conducted an analysis of nine prospective studies over period of 11 years including 720,425 participants who experienced total of 25,769 cardiovascular events. Median follow-up came to 11 years. In that study, researchers found that participants who reported the highest sedentary times (mean 12.5 h/day) had an increased risk for CVD (HR 1.14) compared with participants who reported the least amount of sedentary time (mean 2.5 h/day). [10]



Television-Watching Health Effects Worse Than Other Sitting

• To assess whether some sedentary activities are more harmful than others, researchers analyzed data from the long-term Coronary Artery Risk Development in Young Adults (CARDIA) study. The CARDIA researchers followed 5115 black and white men and women who were 18 to 30 years of age in 1985 and 1986. All lived in Birmingham, Alabama; Chicago; Minneapolis; or Oakland, California. They assessed effect of following activities on development of metabolic syndrome: commuting in the bus,



watching TV, working on computer, doing paper work, reading and using a phone. From those activities, watching TV was most strongly associated with risk of metabolic syndrome. One possible explanation is that while watching TV we move the least. [11]

All activity can cut risk of heart failure

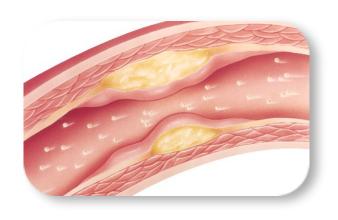
- All activity levels can cut the future risk of heart failure (weakening or stiffening of heart muscle)
- Both moderate and high levels of activity are associated with a reduced risk.
- The protective effect may be due to exercises effects on other heart failure risks such as blood pressure, lipids, insulin sensitivity and body weight. [12]

Exercise and your arteries

• Exercise produced a clear antiatherosclerotic (preventing plaque buildup) effect. [13]

Regular exercise can prevent age related stiffening of heart muscle.

Exercise 4 to 5 times per week throughout adulthood prevented age related stiffening of the heart muscle. The effect was even more



pronounced in competitive masters athletes that exercised 6 to 7 times a week. (left ventricular stiffening has been implicated in conditions such as diastolic heart failure and atrial fibrillation.) Of note, casual exercise (2 to 3 times per week had no effect). [14]

Exercise weakens the link between obesity and heart damage!

- Even though heavy adults can be more prone to cardiac problems than their slimmer peers, exercise may lower the odds of heart damage for obese people.
- A 2017 study of 9500 participants found that obese and inactive individuals had higher levels of cardiac-troponin T (cTNT) that is a marker of heart muscle damage. Rising levels of this protein can be an early warning of future heart failure in people who don't have symptoms.



- Overall, 7.2 percent of the participants had elevated levels of cTNT. Compared to non-obese people who got at least 75 minutes of vigorous exercise or 150 minutes of moderate intensity activity each week, sedentary obese people were about 2.5 times more likely to have high levels of cTNT.
- However obese people who met the same recommended exercise targets, as their non-obese counterparts were only 68 percent more likely to have elevated cardiac troponin T levels.
- This suggests that physical activity prevents at least some of the heart damage associated with obesity. [16]

Benefits of exercise may outweigh impact of obesity on cardiovascular disease!

This observational study was conducted in more than 5,000 people aged 55 years and older who were followed-up for 15 years. During the 15-year follow-up, 16 percent of participants had a cardiovascular event. When analyzed alone, physical activity was associated with a decreased risk of cardiovascular disease regardless of BMI category. There was no association between BMI alone and cardiovascular disease. Compared to normal weight people with high physical activity levels (the ideal), overweight or obese individuals with high levels of physical activity were not at increased risk of cardiovascular disease. But overweight or obese people with low levels of physical activity had 1.33 and 1.35 times higher risk for developing cardiovascular disease, respectively. [17]

Increased physical activity associated with lower risk of 13 types of cancer.

A recent study of the relationship between physical activity and cancer has shown that greater levels of leisure-time physical activity were associated with a lower risk of developing 13 different types of cancer. The risk of developing seven cancer types was 20 percent (or more) lower among the most active participants (90th percentile of activity) as compared with the least active participants (10th percentile of activity). This study pooled data on 1.44 million people, ages 19 to 98, from the United States and Europe, and was able to examine a broad range of cancers, including rare malignancies. Participants were followed for a median of 11 years during which 187,000 new cases of cancer occurred. The investigators confirmed that leisure-time physical activity, as assessed by self-reported surveys, was associated with a lower risk of colon, breast, and endometrial cancers, (most common cancer of the uterus) esophageal adenocarcinoma, liver cancer, stomach cancer, kidney cancer, myeloid leukemia, myeloma, cancers of the head and neck, rectum, and bladder. [18]

Exercise Capacity is the best predictor of your mortality!

- Exercise capacity is inversely associated with all-cause mortality in older men.
- Most health benefits are evident at fitness levels above five metabolic equivalents (METs), which is a measure of physical endurance.
- This can be accomplished with 20 to 40 minutes of brisk daily exercise.
- For each MET increase, there is a 12 percent reduction in risk of all-cause mortality. [19]

Bike to work!

- A 2017 study published in the British Medical Journal observed 250,000 UK commuters over a five-year period. The cyclist averaged about 30 miles per week.
- Those who cycled to work reduced their risk of death by 41 percent, and the incidence of cancer and heart disease by 45 and 46 percent respectively! [20]



Which Exercise is best for Aging Muscles?

- As our muscles age, the mitochondria (microscopic power plants) in the cells begin to malfunction and their numbers declines. This causes the muscle cells to become weaker.
- A twelve week 2017 study, including 72 sedentary men and women was conducted to look at what types of exercise are best for reversing the age-related damage mitochondrial by activating genes specific for metabolism.



Three exercises included:

- vigorous weight training several times a week
- interval training three times a week (4 minutes maximum intensity, 3 minutes rest, 3 times)
- moderate pace bicycling on a stationary bike a few times a week and weight lifting the rest of the days
- For individuals younger than 30, results showed that activity levels changed in 74 genes for weight lifters, 170 genes for moderate exercisers, and 274 genes for interval training!
- Individuals over 60 saw a 19 gene change in moderate exercising, 33 gene change in weight lifters and a 400 gene change in interval trainers! [21]

To Maintain Muscle and Lose Fat as You Age, Add Weights

Two common types of bench pressing

Which one works for weight loss?

249 participants who were overweight or obese and sedentary were randomly assigned the volunteers to one of three groups, calorie reduction alone, calorie reduction aerobic exercise (brisk walking on a track 45 min, four times a week), calorie reduction and a full body resistance training using weight machines). Program was continued for 18 months; the men and women in the group that had cut calories but not worked out had lost an average of about 12 pounds each.

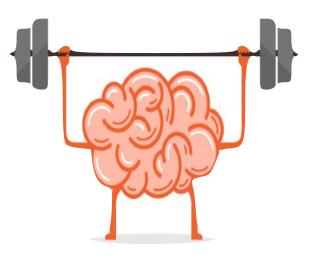


Those who had cut calories and walked had dropped far more weight, about 20 pounds each, while those who had dieted and weight trained likewise had lost about 20 pounds per person. But the weight loss among walkers and weight trainers was qualitatively different. Their new body-compositions scans showed, the weight trainers had lost about two pounds of muscle and 18 pounds of fat, while the walkers had dropped about four pounds of muscle and 16 pounds of fat. [22]



Exercise and your Brain

- Older individuals who exercised on regular basis experienced hippocampus growth and improvements in spatial memory. [23]
- Hippocampus functions involve short-term memory and spatial navigation.
- There is a direct relationship between exercise and hippocampus size and memory in humans.



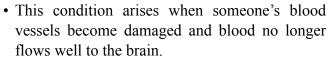
- Exercise such as walking at least 6-9 miles week was associated with 50 percent decreased risk of dementia and slowed down progression of dementia if already present. [24]
- Exercise, including running, results in production of protein cathespin B by skeletal muscles.
- Cathespin B production enhances the expression of the brain-derived neurotrophic factor (BDNF) and doublecortin (DCX). Those chemicals in turn promote neurogenesis (growth of new brain cells) and cognition in the hippocampus. Each neuron has 10,000 connections. [25]
- A 2016 study published in Neurology found that exercise during your midlife exercise might benefit brain size later on
- About 1,000 participants preformed a treadmill test at average age 40 and then an MRI of the brain was performed two decades later. Results found that participants with poor fitness and higher blood pressure and heart rate at baseline had smaller brain volume after two decades.
- A decrease in brain volume (shrinking brain) is a obviously strong indicator of cognitive decline. [26]
- Dancing may be the best exercise for older adults! A 2017 study published in Frontiers in Aging Neuroscience, with 174 healthy participants between ages 60-70, found that compared to walking or stretching the dancers actually had increased white brain matter in their fornix.
- The fornix is responsible for processing speed and memory.
- This change may be due to the fact that dancing requires a person to learn, master and remember choreography, which is more cognitive demand than walking and stretching.
- This white matter growth translated to better performance on cognitive and thinking tests. [27]

Another, just discovered benefit of exercise: self-control:

• Study subjects were asked to participate in a two-month walking and jogging regimen 3 x a week for 45 minutes supervised by a coach, who encouraged them to maintaining pace that felt difficult but sustainable. Participants were explained that this program was to enhance their fitness and were not informed of the true purpose of the study.

• Most of the participants gained a notable degree of self-control, based on their questionnaires, after completing the walking and jogging program. Not surprisingly, the increases were proportional; the more sessions a participant attended or the more her average jogging pace increased, the greater the improvement in her delay-gratification score. This effect persisted for 1 month after the training session. [28]

Exercise and vascular dementia (second most common form of dementia in adults)





- It is often associated with high blood pressure and heart disease.
- One of the particular hallmarks of vascular dementia in its early stages, researchers have found, is that it tends to make the brain function less efficiently.
- MRI scans of individuals with a diagnosis of vascular cognitive impairment demonstrated more neural activity in parts of their brains that are involved with memory, decision-making and attention than did people without the disease, indicating that their brains had to work harder during normal thinking than healthier brains did.
- Just walking 3 x a week for 1 hour improved brain efficiency and thinking skills. The improvement was already seen after 6 months of walking! [29]

Nonrecreational Physical Activity Reduces Death, CV Events

The PURE, which involved 130,843 individuals without pre-existing CV disease from 17 countries who were followed for almost 7 years, extends existing knowledge on the benefits of physical activity in high-income countries to low- and middle-income countries.

The researchers explained that studies investigating the role of physical activity in preventing death from CV disease have been primarily from high-income countries and focused on recreational or leisure time physical activity. In low-income and middle-income countries, physical activity is predominantly from non-recreational activities, such as transportation, occupation, and housework, and these have not been well studied before.

Results showed that compared with low physical activity (<150 minutes of moderate-intensity exercise per week), moderate (150 to 750 minutes per week) and high (>750 minutes per week) physical activity were associated with graded reduction in mortality: 20 percent reduction for moderate and 35 percent reduction for high level.

Interestingly, PURE concluded that high physical activity was only possible in people who completed physical activity as form of transport, part of their job or trough housework. Otherwise who has more than 12.5 hours a week to go the gym???? Not me! [30]

Exercise at the Workplace: No benefit if your job is source of stress, you are dissatisfied, underpaid and your boss is an ass...

- Recently, studies have found that physical activity during work hours does not always benefit you.
- A 2015 study published in the European Journal of Preventive Cardiology including about 12,000 nurses found that although exercising during leisure time and ischemic heart disease (IHD) has an inverse relation; exercising intensity during work and IHD actually has a U-shaped association.
- Nurses were at the highest risk for IHD when they were sedentary during work and leisure time and also when they were highly active at work and sedentary during leisure time. Patients had less of a risk when they had moderate physical activity at work and vigorous activity during leisure time. [31]
- A 2005 study published in the British Medical Journal that looked at 800 employees concluded that compared to those with low job strain those who
 - reported having high job strain and work demands had a 2.2 fold increase in risk for cardiovascular mortality. [32]
- In a 2015 study about 5,000 industrial male workers reported their work physical activity and their leisure time physical activity. Results found that those with moderate-vigorous work activity had an increased risk of all-cause mortality. Those who had light or no work place physical activity and high leisure time activity had the lowest risk. [33]







Exercise and Mood: Try if first before taking antidepressants!

Anxiety

• Exercise training helps anxiety symptoms. A 2010 article reviewed multiple studies evaluating effects of exercise on anxiety. Symptoms were reduced by 29 percent compared to no intervention. Exercise training programs lasting no more than 12 weeks, using session durations of at least 30 minutes, resulted in the largest anxiety improvements. [34]

Depression

- Growing body of research suggests that one of its best cures is cheap and ubiquitous. In 1999, a randomized controlled trial showed that depressed adults who took part in aerobic exercise improved as much as those treated with Zoloft.
- A 2006 meta-analysis of 11 studies bolstered those findings and recommended that physicians counsel their depressed patients to try it.
- A 2011 study took this conclusion even further: It looked at 127 depressed people who hadn't experienced relief from SSRIs, a common type of antidepressant, and found that exercise led 30 percent of them into remission a result that was as good as, or better than, drugs alone. Keep in mind that recent research questioned benefits of antidepressant medications known as SSRI in mild to moderate depression (not better than placebo!) [35]

Should you eat before exercising? NO!

- A 2017 study involving 10 overweight and sedentary males looked at whether fasting or eating before exercise was better on overall health.
- The men walked for an hour on the treadmill at a moderate pace on two separate mornings. On one occurrence the men exercised after fasting for the night and the second time the men ate a 600-calorie meal two hours before exercising including toast, jam, cereal, milk and orange juice.
- Results showed that when looking at the fat cells of the men, the genes responsible for improved regulation of blood sugar and insulin levels were much more active when fasting before exercise. [36]

Marathon Running

- There are conflicting data on effect of endurance exercise and risk for coronary artery disease. Recently those concerns have been put to rest.
- Marathoners are not at increased risk for narrowing or hardening of the arteries (atherosclerosis).



- Researchers tested the arteries of 97 runners who had competed in an average of 11 long races, such as half marathons, marathons and ultramarathons. They ran 36 miles weekly and 1,018 miles annually, on average.
- There was no evidence of a link between long distance running and atherosclerosis, according to the study.
- Age was the only characteristic independently associated with the health of the runners' arteries. (You cant outrun your age!)
- Marathon running itself is not a risk factor for atherosclerosis. It appears that you can run as many marathons as you want and not be in danger of developing impaired blood vessel function or atherosclerosis. [37]
- Most recent study however found that endurance athletes despite having age related calcium build up actually did not developed myocardial infarction (heart attack). It seems that their plaques are more benign and their vessels increased in size to accommodate extra blood flow during the run compensating for the plaque buildup!
- The analysis, published online in Circulation on April 27, 2017, of almost 300 middle-aged male athletes showed that endurance athletes with the highest levels of physical exercise had a 47 percent increased risk of developing CAC and a 56 percent increased prevalence of plaque. But they were 3.5 times more likely to have plaques with the lower-risk composition. (less likely to rupture and lead to heart attack) [38]

Who is more likely to die during marathon?

Answer: not the runners!

 Researchers at Harvard Medical School have established that people who suffer a heart attack when there is a marathon taking place nearby have a 15 percent higher chance of dying within the next month than if the episode struck on a non race day.



• They found that, despite the legion of emergency services personnel usually present along the 26.2-mile route, the traffic is often so clogged up by road closures that crucial minutes are lost getting patients to hospital. Published in the New England Journal of Medicine, the study showed that ambulance transport to hospital was delayed by an average of 4.4 minutes on marathon days! [39]

Like everything else in life, moderation may apply to exercise - specifically jogging!

Copenhagen City Heart Study evaluated 1,098 healthy joggers and 3,950 healthy non-joggers:

- Light jogging was defined as a slow or average pace (approximately 5 mph), three or fewer times per week, for less than 2.5 hours total per week.
- Moderate jogging was defined as a slow or average pace, three or fewer times per week, but for 2.5 hours or more per week. (Moderate jogging was also defined as a faster pace, more than three times per week, or 4 hours or less per week.)
- Strenuous jogging was defined as running at a fast pace (>7 mph), more than 3 times per week, and 4 hours total per week.

The following association between mortality and jogging duration/intensity compared with non-joggers was observed:

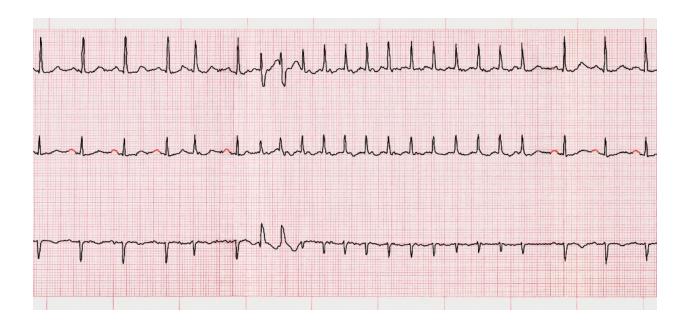
- Joggers who ran 1 to 2.4 hours per week had the lowest risk of mortality, with a significant 71 percent lower risk of death than sedentary non-joggers.
- Individuals who ran less than 1 hour per week had a significantly 53 percent lower risk of all-cause mortality. In contrast, compared with the sedentary group, those who ran 2.5 to 4 hours per week or more than 4 hours per week did not have a lower risk of mortality.
- Regarding frequency, the optimal dose of jogging was two to three times per week. These joggers had a significantly 68 percent lower risk of death compared with the healthy sedentary group. Even those who ran once per week had a significantly lower risk of death compared with non-joggers those who jogged three or more times per week did not.
- In terms of pace, slow-paced joggers had a significantly 49 percent lower risk of death compared with sedentary non-joggers. The fastest runners those who covered more than 7 mph had the same mortality risk as sedentary non-joggers. [40]

Strenuous Exercise as trigger for Atrial Fibrillation and Heart Attack

 According to the American Heart Association and the American College of Cardiology, there is 25 percent decrease in risk of developing atrial fibrillation with moderate exercise compared to sedentary individuals.

BUT IF you overdo:

• This differs for intense exercise for men over 40 years old. A 2017 study concluded that when men (ages 40-60) exercise at a high intensity for more than 5 hours a week and are at 80 percent of their maximum heart rate, they are actually increasing their chance of atrial fibrillation 10-fold. Interestingly, probably due to a different shape of the left atrium risk of atrial fibrillation was not increased in women. [41]



Exercise as trigger of heart attack (myocardial infarction)

• Strenuous activity, especially in individuals not accustomed to exercise can trigger heart attack by causing plaque rupture (see chapter 1). Classic example is snow shoveling first reported in medical literature to cause death by coronary thrombosis in 1937! [42]

References:

- 1. Morris, J.N., et al., *Coronary heart-disease and physical activity of work*. Lancet, 1953. **265**(6795): p. 1053-7; contd.
- 2. Services, U.S.D.o.H.a.H. *Recommendations for Physical Activity NHLBI, NIH.* 2016; Available from: https://www.ncbi.nlm.nih.gov/pubmed/.
- 3. Services, U.S.D.o.H.a.H., Why Join My Go4Life? National Institute on Aging, 2014.
- 4. Prevention, C.f.D.C.a., *How much physical activity do adults need?* | *Physical Activity* | *CDC*. 2015.
- 5. LaMonte, M.J., et al., *Accelerometer-Measured Physical Activity and Mortality in Women Aged 63 to 99.* J Am Geriatr Soc, 2017.
- 6. O'Donovan, G., et al., Association of "Weekend Warrior" and Other Leisure Time Physical Activity Patterns With Risks for All-Cause, Cardiovascular Disease, and Cancer Mortality. JAMA Internal Medicine, 2017. 177(3): p. 335-342.
- 7. Oja, P., et al., Associations of specific types of sports and exercise with all-cause and cardiovascular-disease mortality: a cohort study of 80 306 British adults. Br J Sports Med, 2017. **51**(10): p. 812-817.
- 8. Tigbe, W.W., et al., *Time spent in sedentary posture is associated with waist circumference and cardiovascular risk.* Int J Obes (Lond), 2017. **41**(5): p. 689-696.
- 9. Biswas, A., et al., Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med, 2015. **162**(2): p. 123-32.
- 10. Ryu, S., et al., *Relationship of sitting time and physical activity with non-alcoholic fatty liver disease.* J Hepatol, 2015. **63**(5): p. 1229-37.
- 11. Pandey, A., et al., *Continuous Dose-Response Association Between Sedentary Time and Risk for Cardiovascular Disease: A Meta-analysis.* JAMA Cardiol, 2016. **1**(5): p. 575-83.
- 12. Harrison, L., *Television-Watching Health Effects Worse Than Other Sitting*. Medscape Medical News, 2017.
- 13. Wang, Y., et al., *Occupational, commuting, and leisure-time physical activity in relation to heart failure among finnish men and women.* J Am Coll Cardiol, 2010. **56**(14): p. 1140-8.
- 14. Szostak, J. and P. Laurant, *The forgotten face of regular physical exercise: a 'natural' anti-atherogenic activity.* Clin Sci (Lond), 2011. **121**(3): p. 91-106.
- 15. Bhella, P.S., et al., *Impact of lifelong exercise "dose" on left ventricular compliance and distensibility.* J Am Coll Cardiol, 2014. **64**(12): p. 1257-66.
- 16. Florido, R., et al., *Physical Activity, Obesity, and Subclinical Myocardial Damage*. JACC Heart Fail, 2017. **5**(5): p. 377-384.
- 17. Koolhaas, C.M., et al., *Impact of physical activity on the association of overweight and obesity with cardiovascular disease: The Rotterdam Study.* Eur J Prev Cardiol, 2017. **24**(9): p. 934-941.
- 18. Moore, S.C., et al., Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. JAMA Intern Med, 2016. **176**(6): p. 816-25.
- 19. Myers, J., et al., *Exercise capacity and mortality among men referred for exercise testing*. N Engl J Med, 2002. **346**(11): p. 793-801.

- 20. Celis-Morales, C.A., et al., *Association between active commuting and incident cardiovascular disease, cancer, and mortality: prospective cohort study.* Bmj, 2017. **357**: p. j1456.
- 21. Robinson, M.M., et al., Enhanced Protein Translation Underlies Improved Metabolic and Physical Adaptations to Different Exercise Training Modes in Young and Old Humans. Cell Metab, 2017. **25**(3): p. 581-592.
- 22. Beavers, K.M., et al., Effect of Exercise Type During Intentional Weight Loss on Body Composition in Older Adults with Obesity. Obesity (Silver Spring), 2017. **25**(11): p. 1823-1829.
- 23. Erickson, K.I., et al., *Aerobic fitness is associated with hippocampal volume in elderly humans*. Hippocampus, 2009. **19**(10): p. 1030-9.
- 24. Erickson, K., et al., *Physical activity predicts gray matter volume in late adulthood: The Cardiovascular Health Study(e–Pub ahead of print)*, in *Neurology*. 2010. p. 1415-22.
- 25. Moon, H.Y., et al., Running-Induced Systemic Cathepsin B Secretion Is Associated with Memory Function. Cell Metab, 2016. **24**(2): p. 332-40.
- 26. Spartano, N.L., et al., *Midlife exercise blood pressure, heart rate, and fitness relate to brain volume 2 decades later.* Neurology, 2016. **86**(14): p. 1313-9.
- 27. Burzynska, A.Z., et al., White Matter Integrity Declined Over 6-Months, but Dance Intervention Improved Integrity of the Fornix of Older Adults. Front Aging Neurosci, 2017. 9: p. 59.
- 28. Sofis, M.J., A. Carrillo, and D.P. Jarmolowicz, *Maintained Physical Activity Induced Changes in Delay Discounting*. Behav Modif, 2017. **41**(4): p. 499-528.
- 29. Hsu, C.L., et al., Aerobic exercise promotes executive functions and impacts functional neural activity among older adults with vascular cognitive impairment. Br J Sports Med, 2017.
- 30. Lear, S.A., et al., *The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study.* Lancet, 2017.
- 31. Allesoe, K., et al., *High occupational physical activity and risk of ischaemic heart disease in women: the interplay with physical activity during leisure time.* Eur J Prev Cardiol, 2015. **22**(12): p. 1601-8.
- 32. Kivimaki, M., et al., *Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees.* Bmj, 2002. **325**(7369): p. 857.
- 33. Harari, G., M.S. Green, and S. Zelber-Sagi, *Combined association of occupational and leisure-time physical activity with all-cause and coronary heart disease mortality among a cohort of men followed-up for 22 years*. Occup Environ Med, 2015. **72**(9): p. 617-24.
- 34. Herring, M.P., P.J. O'Connor, and R.K. Dishman, *The effect of exercise training on anxiety symptoms among patients: a systematic review.* Arch Intern Med, 2010. **170**(4): p. 321-31.
- 35. Khazan, O., For Depression, Prescribing Exercise Before Medication. The Atlantic, 2014.
- 36. Chen, Y.C., et al., *Feeding influences adipose tissue responses to exercise in overweight men.* Am J Physiol Endocrinol Metab, 2017. **313**(1): p. E84-e93.
- 37. Cardiology, E.S.o., *Running multiple marathons does not increase risk of atherosclerosis*. Science Daily, 2017.

- 38. Aengevaeren, V.L., et al., *Relationship Between Lifelong Exercise Volume and Coronary Atherosclerosis in Athletes.* Circulation, 2017. **136**(2): p. 138-148.
- 39. Jena, A.B., et al., *Delays in Emergency Care and Mortality during Major U.S. Marathons*. N Engl J Med, 2017. **376**(15): p. 1441-1450.
- 40. Schnohr, P., et al., *Dose of jogging and long-term mortality: the Copenhagen City Heart Study.* J Am Coll Cardiol, 2015. **65**(5): p. 411-9.
- 41. al, N.A.E.e., *Atrial Fibrillation in Athletes: A Lesson in the Virtue of Moderation ScienceDirect.* JACC: Clinical Electrophysiology, 2017. **3**(9).
- 42. MASTER, A.M., S. DACK, and H.L. JAFFE, *FACTORS AND EVENTS ASSOCIATED WITH ONSET OF CORONARY ARTERY THROMBOSIS*. Journal of the American Medical Association, 1937. **109**(8): p. 546-549.

Vedic Wisdom

What is Fear?

Unacceptance of uncertainty, If we accept that uncertainty It becomes—Adventure

What is Anger?

Unacceptance of things, which are beyond our control,
If we accept it becomes—Tolerance

What is Envy?

Unacceptance of good in others If we accept that good, It becomes—Inspiration

What is Hatred?

Unacceptance of person as he is, If we accept person unconditionally, It becomes—Love

Destructive Effects of Negative Thoughts

Anatomy of Stress

The limbic system (reptile brain) is a portion of the brain that is directly responsible for controlling individuals' emotional responses.

The limbic system includes:

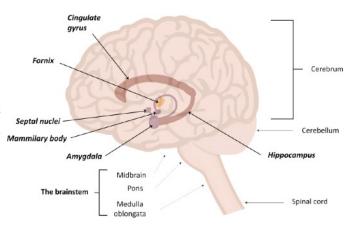
Hippocampus: involved in long-term memory and compares and detects present threats with past experiences.

Amygdala: responsible for the response to emotions including fear, anger and pleasure, especially negative stimuli.

Hypothalamus: regulates body temperature, thirst, hunger and involved in sleep and emotional activity.

When we are faced with a stressful situation, information is first sent to the amygdala where the information is interpreted and then sent to the hypothalamus. The hypothalamus then activates a part of the autonomic nervous system called the sympathetic nervous system which triggers a fight or flight response. Epinephrine is released from the body and causes an increase in pulse, breathing rate and blood pressure. Senses including sight and hearing are heightened and blood sugar and fat are released into the bloodstream to provide extra energy to the body.

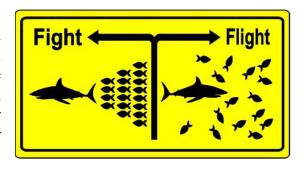
The Limbic System



If the threat continues the HPA axis (The hypothalamic-pituitary-adrenal axis) is activated which causes cortisol to be released to keep the body in fight or flight more. The hypothalamus releases corticotrophin-releasing hormone (CRH), which then leads to the release of adrenocorticotropic hormone (ACTH), which ultimately leads to the release of cortisol. People who under chronic stress have continuous activation of the HPA axis leading to weight gain, high blood pressure, increased risk of heart attack and stroke, memory loss, depression, anxiety and a permanent disconnect between the primitive and smart brain. Long-term stress causes degeneration of the prefrontal cortex and hippocampus, which results in inhibiting their control over the stress response. [1], [2]

Simplified explanation of fight and flight response.

Primitive brain: continuously monitors for dangers. Not much thinking involved but rapid reaction ("reptile brain"). Smart brain (abstract thinking, slow to respond), controls (suppresses) primitive brain. During a dangerous situation, smart brain disconnect form primitive brain, which takes over and responds immediately, around 30 seconds later smart brain returns online to reassess situation. Example, you walk through a forest and see an



angry bear: rather than trying to figure out, why is this creature angry, you run without further thinking. Once you reached a safe distance, smart brain assumes the driver seat and reassesses the situation. This was given to us by nature as survival tool but we tend to abuse it: for example while driving in the traffic, rapidly changing lanes and honking, watching news, screaming at kids etc. Keep in mind that primitive brain is so dumb that it can't tell the difference between reality and fiction: that's why we jump watching horror movies. In addition, smart brain continuously generates thoughts regarding possible future scenarios:" If my boss tells me tomorrow to do extra work and will tell him what I really think and quit!" The primitive brain as threat perceives this and triggers fight and flight response, smart brain disconnects and our logical thinking stops....

During chronic stress however, we may permanently lose connection between smart and primitive brain. We start functioning using predominantly reptilian brain and all our responses are either fight or flight. We become angry and stressed out and impossible to be around... In addition, as primitive brain does not need much memory to operate on (as we switched to survival mode only) and start losing memory/ Midlife stress is a strong predictor for dementia in older age...

Stress and negative thoughts will kill your memory.... [3]

- Women who had been through significant stressors in mid-life had a significantly (65%) greater risk of developing dementia later on.
- The theory is that stressful events can trigger a cascade of reactions involving the stress hormones (glucocorticoids) and eventually leading to atrophy in the brain's hippocampus the region that is the seat of memory, and known to be most affected by Alzheimer's disease.
- Amyloid-beta plaques (or "brain gunk") have been shown to accumulate following increased



brain cell activity. Specifically, there's evidence that people who have more activity in their default mode networks (which is linked to depression, mind-wandering, and general unhappy thoughts, among others) may have increased risk for Alzheimer's disease precisely because of this connection. This suggests, somewhat alarmingly, that even our thoughts and moods may affect our risk for dementia.

Depression

- A study of about 150 patients found that those who had depression symptoms also had impaired endothelial (blood vessel) function. (Vessels don't relax)
- Men who are persistently depressed are 2.36 times as likely to have high coronary calcium, leading to atherosclerosis or blocked arteries. [4]



- Elevated levels of inflammation throughout the cardiovascular system were found in physically healthy patients with depression. [5]
- Patients with both heart disease and depression have a higher risk of dying. [6]
 - ▶ All death from any cause: three times higher risk
 - ▶ Heart disease mortality: four times higher risk
- Patients hospitalized heart failure who also had moderate to severe depression were five times as likely to die within a year of leaving the hospital if their depression did not improve. [7]
- Clinical depression affects 24-42 percent of heart failure patients. [8]
- A 2009 study that included 289 middle-aged twins found a link between major depression and coronary reserve flow which is defined as "the ratio of maximum flow during stress to flow at rest measured in milliliters per minute per gram of tissue".
- The study concluded that the coronary flow reserve was 14 percent lower in the twins with depression than in their brothers without depression for twins. [9]

Anxiety

• Anxiety is an independent predictor of coronary heart disease. It has been associated with the development of heart disease in initially healthy people. [10] Part of this relationship may be explained by an individual's behavior such as smoking, alcohol consumption and lack of exercise. [11]



- Patients with stable heart disease and increased levels of anxiety are more likely to experience a cardiovascular event, such as stroke, heart attack or death.
- Generalized anxiety disorder is associated with a 62 percent increased risk for poor cardiovascular outcomes. [12]
- Anxious patients may be less likely to seek care due to their avoidant coping strategy.
- Anxious people have about a 25 percent increased risk of cardiac heart disease and nearly a 50 percent higher risk of cardiac death later on in life. [10]

Depression after Stroke and Heart attack

One in 5 people hospitalized for heart attack or chest pain develop major depression -- about four times the rate in the general population, according to the American Heart Association. [13]

- One in 3 stroke survivors become depressed, [14] along with up to half of those who undergo heart bypass surgery. [15] Heart disease patients who become depressed are twice as likely to die within the following decade as other patients, according to an unpublished study presented in March 2107 at the American College of Cardiology's annual meeting.
- Depression increased the risk of death more than any other risk factor in the study, even smoking! Most often, depressed heart attack survivors die of physical causes, partly because they're less motivated to take care of themselves and take medication as directed. [16]

Yet only 48 percent of heart attack survivors with depression receive treatment.....

Why cardiac rehab is so important after heart attack?

Only 2 out of 3 patients will be referred to cardiac rehab after heart attack, just 23 percent of patients attended one or more sessions, and 5 percent completed all 36 recommended sessions. [17] Cardiac rehab programs include stress management and teach relaxation techniques and coping skills similar to those used in some types of depression therapy. The programs can reduce the risks of heart attack more than standard rehab. In a three-year study, which included heart patients ages 36 to 84, nearly half of patients who didn't attend cardiac rehab died or had a heart attack, stroke or hospitalization due to chest pain, compared with 33 percent of those who attended rehab. Among those whose rehab included stress management, only 18 percent suffered one of these heart-related complications, the study found. [18]

Ask your doctor, if you are eligible for cardiac rehab and don't take "You don't need it" for an answer!

Stress

- A 2013 study that observed about 7,300 individuals found that those who reported having stress impact their health severely had a 2.12 higher risk of coronary death or non-fatal heart attacks. [19]
- Emotional stress causes increased amygdala activity in the brain. The amygdala is the portion of the brain that responds to emotionally charged or negative stimuli. This brain activity



from stress can increase bone-marrow activity and arterial inflammation, which is associated with cardiovascular events. [20]

• Chronic stressors that lead to coronary artery disease include low social support, marital stress, work strain, low socioeconomic status, and caregiver stress. These stressors are much harder to control compared to lifestyle factors including unhealthy diet, smoking and lack of physical activity. [21]

Stress and Family

- In a study of over 4,500 people, it was found that demands of intimate family ties and worries that arise within families can increase the risk of angina (chest pain).
- When the source of worries was...
 - ▶ A spouse or partner, the risk increased three-fold.
 - ▶ Children, the risk increased two-fold.
- Demands from more distant relations resulted in no increased risk. [22]

Stress at Work

- Work-related stressful life events seem to be possible triggers of a heart attack. A highpressure deadline at work increases the chance of heart attack within 24 hours six-fold.
- Men are 80 percent more likely to have a heart attack if they experience a stressful work situation in the previous 12 months.
- A change in financial circumstances triples the risk for heart attack in females.



• After receiving more responsibilities at work both men and women were six times more likely to have a heart attack. [23]

Stress and cancer

• In modern lifestyle societies, chronic stress has been associated with the pathogenesis of many diseases, including cancer. Chronic stress results in the activation of specific signaling pathways in cancer cells and the tumor microenvironment, leading to tumor growth and progression (metastasis). [24]

Severe Stress Linked to Lupus

Researchers studied 54,763 women enrolled in a larger health study. They used questionnaires to determine exposure to trauma, including serious car accidents and sexual assault, and examined medical records to find diagnoses of post-traumatic stress disorder. Over the 24 years of the study, they found 73 cases of lupus.

Compared to women without trauma, women with PTSD were almost three times as likely to have lupus. Exposure to trauma, even without having symptoms of PTSD, more than doubled the risk of developing the disease. [25]

Posttraumatic Stress Disorder (PTSD)

- 15 percent of individuals diagnosed with acute coronary syndromes (heart attacks) develop PTSD. [26]
- A 2011 study including 247 patients hospitalized for an acute coronary syndrome found that those with high intrusion symptoms of PTSD (thoughts or images related to the traumatic event, nightmares, and flashbacks) had a 3-fold greater risk of a cardiac event or death within 42 months of hospitalization. [27]



- Compared to women who have not experienced a traumatic event, women who have four or more PTSD symptoms have a 60 percent higher risk of cardiovascular disease. [28]
- A 2013 study of 400,000 participants showed that PTSD could increase your risk of cardiac events by 27 percent. [29]
- The relative risk of stroke for individuals with PTSD is increased to 2.36 according to a 2016 study with over 2,000,000 participants. [30]
- A study including 65,603 male and 6,964 female veterans who had PSTD found that the odds ratio for having hypertension was 2.88 for both. [31]
- The same study showed the odds ratio for hyperlipidemia was 2.7 and 2.68 for men and women respectively. [31]
- PTSD is associated with an increased risk of death from any cause and an increased risk of developing cardiovascular disease.
- A study of over 286,000 veterans showed that those with PTSD had twice the risk of death.
- Twenty-eight percent of veterans who died of heart disease had PTSD.
- In those who did not die, only 8.1 percent had PTSD. [32]



Anger: Most Powerful Risk Factor Ever!

- If you experience intense road rage your risk of stroke increases fourfold and your risk of heart attack increases fivefold in the two hours following the episode. [33]
- Your risk of a heart attack increases 2.4-fold after an episode of anger. [34]
- In a 2016 study of 12,461 participants, 14.3 percent of the individuals were upset or angry in the hour before their heart attack. [35]
- A study including about 1200 individuals with defibrillators observed how many people experienced shocks from cardiac arrest after experiencing an episode of anger. Those who experienced moderate anger had a 3.2-fold increase of experiencing cardiac arrest while those who were furious had. [36]
- For individuals with a low risk of heart disease, getting angry once a day can lead to one extra heart attack per 10,000 people per year. Those who get angry five or more times a day increases to 4 heart attacks per 10,000 people per year.
- For individuals with a high risk of heart disease, those getting angry once a day would lead to an extra 158 heart attacks and getting angry 5 times a day would lead to an extra 657 heart attacks per 10,000 people per year. [33]
- Conclusion: nature does not appreciate angry individuals and takes them out of circulation!

• You are better off to be a happy smoker than non-smoking jerk!



Or



- Patients reporting anger, stress or depression within two hours of the onset of coronary symptoms showed heightened platelet activity. [37]
- Moderate anger increased the risk of shock from a defibrillator (to treat a fatal heart rhythm, like ventricular tachycardia or ventricular fibrillation) 3.6 times and when person become furious risk of shock increased 16 times!!!! [36]

Stress cardiomyopathy (also known as broken heart syndrome or Takotsubo cardiomyopathy)

- You don't have to wait for months or years to experience effect of stress on your heart.
- Sudden intense emotion such as learning about death of spouse, being involved in car accident, heated argument etc. release very high levels of catecholamines (adrenaline), which stuns the heart muscle, leading to sudden onset of heart failure (weakening of heart muscle).
- It affects predominantly postmenopausal females (90%) and the heart muscle recovers over time.



- Symptoms may be very similar to that of a heart attack. [38]
- Of interest, sudden positive emotions can trigger it as well! In 2016 researchers even coined a term "Happy Heart Syndrome". Positive events that triggered stress cardiomyopathy were for example, birthday party, becoming great grandmother, sons wedding, winning jackpot in casino, unexpected visit form favorite nephew etc. [39]

- So think twice before throwing a surprise B day party for your grandma!
- To see how Takotsubo heart looks like check out this Mayo Clinic link on: YouTube[40] (https://www.youtube.com/watch?v=5f2Ga5O55k8)

Next time you celebrate your birthday, load up on aspirin, have 911 on speed dial and be close to a heart hospital!

- The likelihood of experiencing a cardiovascular event on one's birthday is 27 percent higher than on any other day of the year!
- The conclusion was reached by researchers who looked at a very large population of patients presenting to emergency rooms in Ontario, Canada. There were 24,315 ED admissions with acute stroke, 16,088 with TIAs, (transient ischemic attack, also called very incorrectly mini stroke) and 29,090 with acute heart attacks.



• The observed number of vascular events during the birthday was higher than the expected daily number of visits for stroke TIA and acute heart attacks but not for selected control conditions (asthma, appendicitis, head trauma). [41]

"Distressed" Personality [42]

- Type-D personality
- Tendency to experience negative emotions. (eg. anxiety, depression, stress, etc.)
- More unlikely to disclose feelings toward others.
- Often feel a bit insecure.
- More liable to chronic forms of psychological distress.
- Heart disease patients are at a significantly greater risk of adverse cardiovascular events if they have type-D personality.

- They have:
 - ▶ A 3.7 fold increased risk of poor long term prognosis such as mortality, cardiac death and heart attack.
 - ▶ Increased levels of pro-inflammatory cytokines (protein that causes and immune response). This increases the risk of cardiovascular events.
 - ▶ Three-fold increased risk of emotional distress.

Negative thoughts fuel inflammation!

• Cynical distrust, depression and chronic stress were linked with higher levels of inflammation in the cardiovascular system in a study of nearly 7,000 men. [43]

Traumatic Childhood...

• Childhood physical abuse increased risk of heart disease in adulthood by 60 percent even when corrected for adult risk factors such as smoking, hypertension, depression and stress. [44]

Sports fun anyone? Is really not worth dying for it!

- Risk of admission for acute myocardial infarction increased during Soccer World Cup by 25 percent on 30 June 1998 (the day England lost to Argentina in a penalty shoot-out) and the following two days. [45]
- A greater impact is observed in patients with known coronary artery disease and when stressful features are present, including a passionate fan, a high-stakes game, a highintensity game, a loss, and a loss played at home.



- Sporting events affect cardiovascular health through neuroendocrine responses and possibly an increase in high-risk behaviors.
- Acute mental stress increases the activity of the hypothalamic-pituitary-adrenocortical axis and the sympathetic-adrenal-medullary system (activation of fight and flight system) while impairing vagal tone and endothelial function.
- Collectively, these mechanisms increase myocardial oxygen demand and decrease myocardial oxygen supply while also increasing the risk of arrhythmias and thrombosis! [46]

Global events and risk of heart attacks, stress and deaths

There was a transient increase risk of heart attacks, stress cardiomyopathy and shocks from ICD (defibrillator) shortly after terrorist attack on September 11th, 2001 and an earthquake in New Zealand in 2010. [47], [48]

The Power of Mindfulness

Why are we so miserable???

Nature designed us to mainly store negative memories. For every positive memory our mind keeps 5 bad ones? Why? Survival information. Imagine that you have your favorite restaurant, but each time you get there something bad happens, your car was stolen, you got mugged and beaten up... At the end of the day, which is the information more relevant for your survival? The incredibly flavorful cheesecake or missing teeth?

Here is the good news: Neuroplasticity

Neuroplasticity is defined as brain's ability to reorganize itself by forming new neural connections throughout life. Neuroplasticity allows the neurons (nerve cells) in the brain to compensate for injury and disease and to adjust their activities in response to new situations or to changes in their environment. But you can use this process to change your personality and become more positive person. It takes 3-6 months to unlearn a negative and replace it with positive thinking pattern, so get started!

Relaxation Techniques

Tai Chi

Tai Chi is a combination of yoga and meditation. It enhances aerobic capacity, muscular strength, endothelial function and psychological wellbeing.

- Lowers Hypertension and cholesterol.
- It is safe and effective for patients who have had a heart attack, coronary bypass surgery or heart failure. [49]



• Patients with mild or moderate heart failure showed significant quality of life. gains following tai chi classes twice a week. [50]

Yoga

- In a study of 340 men diagnosed with high blood pressure, subjects practiced yoga five days a week for 30 minutes at a time for three weeks. Researchers never called it yoga so as not to discourage the men.
- These men experienced a greater drop in blood pressure (21.1 mm Hg) than the men who only underwent traditional therapy (without yoga). [51]



Yoga and Atrial Fibrillation (AF) episodes

- AF is an abnormal heart rhythm, which may lead to stroke. All negative emotions can trigger atrial fibrillation. [52]
- Taking a 45-minute yoga class three times week is associated with a reduction in AF episodes by 50 percent.
- Twenty-two percent of patients did not have any AF episodes during the part of their life when they were taking yoga classes. [53]

Mindfulness Meditation

How does it work on our brain? Study using functional MRI of the brain (fMRI) demonstrated the following changes in the brain of meditators:

- Focused attention, increased activation in the brain areas implicated in the control and regulation of attention such as prefrontal cortex: less amygdala activation (less emotionally reactive to external events).
- Open monitoring: meditator is able to attend to all stimuli coming at them without getting "stuck" at anything.
- Compassion meditation: involves deliberately generating a state of unconditional compassion and kindness towards all beings, that saturates the whole mind: markedly increased empathy: fMRI: much thicker insula.
- It is official: given overwhelming evidence AHA (American Heart Association) Statement Adds Meditation to Cardiovascular Risk-Reduction Strategies [54]

It takes only 8 weeks of meditation for your brain to start changing! [55]

- A new study shows that those who mediated for 30 minutes a day over an eight-week period showed changes in gray-matter density in areas of the brain pertaining to memory, sense of self, empathy and stress. MRIs showed:
 - ▶ Increased gray matter in the hippocampus area, which is important for learning and memory, reduced gray matter in the amygdala area connected to stress/anxiety.
 - ▶ No changes occurred in the control group (no mediation).
- This was the first study to document these changes over time. [56]
- This technique is based on the Hindu, Buddhist as well as Christian philosophy, transcendental meditation can improve blood pressure, insulin resistance (a condition when insulin is not effective in lowering blood sugars) and cardiac activity. [57]
- In a study of 200 African Americans, participants were asked to meditate regularly. Over nine years, there were 50 percent lower rates of heart attack, stroke and death compared to those who did not meditate. [58]
- Also, the study showed a significant reduction in blood pressure and psychological stress. [58]
- A 2006 study including 103 subjects with coronary heart disease observed how transcendental meditation affects blood pressure, lipoprotein profile, insulin resistance and heart rate variability compared to control subjects receiving health education after 16 weeks. Those who meditated had a 3.4mmHg decrease in blood pressure, and .75 decreases in insulin resistance. [57]
- A 2009 study suggests that meditation reduces blood pressure in cardiac patients. [59], [60]
- A 2007 study found that those who practice mediation have longer attention spans. [61]
- A 2008 study found that people who practiced meditation had a stronger reaction to another
 - person's suffering. They showed stronger activation levels in their temporal parietal junctures, the area of the brain associated with empathy. [62]
- Deep breathing may keep us calm because as we take deep breaths we do not activate out breathing pacemaker, a group of neurons in the brain that controls most aspects of our breathing. If activated, these neurons will send signals to our brain's arousal center, which ultimately may initiate the stress response. [63]



Meditation and Pain

- Mediation has been found to reduce pain unpleasantness by 57 percent and pain intensity ratings by 40 percent. (More effective than morphine!)
- It does this by engaging regions of the brain that alter the way we experience pain. [64]

Meditators May Live Longer [65]

- After a three-month stay at a meditation retreat, people showed higher levels of telomerase, an enzyme associated with longevity. Telomerase is responsible for repairing the structures located on the ends chromosomes, called telomeres. Telomeres prevent the chromosome from unraveling when a cell replicates its DNA to reproduce; it can also slow cell aging.
- Participants meditated six hours per day for three months.
- After the meditation retreat, researchers found that participants had on average about 30 percent more telomerase activity than non-meditating subjects did.
- Higher levels of telomerase have also been associated with psychological improvement.
- In a study on mice, researchers found that higher levels of telomerase reversed signs of aging (restored graying fur and fertility, increased brain size and sharpened scent perception).
- Another study showed that meditation could reduce relapse in patients who are recovering from depression, just as well as antidepressants. [66]

Lifestyle Changes and Telomere Length

- A 2013 study found that changes in diet, exercise and stress management could affect telomere length.
- Telomeres are the caps on the end of our chromosomes. As humans and animals age their telomeres shorten and without telomeres our cells would not be able to divide and would eventually die.
- The study observed 35 men, 25 of which did not partake in a lifestyle change and 10 whom exercised at least 30 minutes a day, ate a Plant-Based or Mediterranean diet and used relaxation techniques such as meditation and prayer to create a positive mental state.
- After five years of this lifestyle, men in the study saw a 10 percent increase in their telomere length compared to the 3 percent decrease in men who did not use the healthy lifestyle stated above. [67]



Meditation and yoga reverses DNA changes caused by stress

When a person is exposed to a stressful event, their sympathetic nervous system responsible for the fight-or-flight response is triggered, in turn increasing production of a molecule called nuclear factor kappa B (NF-kB) that regulates how our genes are expressed. NF-kB translates stress by activating genes to produce proteins called cytokines that cause inflammation at cellular level a reaction that is useful as a short-lived fight-or-



flight reaction, but if persistent leads to a higher risk of cancer, dementia, heart disease accelerated aging and psychiatric disorders like depression. According to the study, however, people who practice relaxation techniques exhibit a decrease in production of NF-kB and cytokines, leading to a reversal of the pro-inflammatory gene expression pattern and a reduction in the risk of inflammation-related diseases and conditions. [68]

Laughter

- Laughter releases nitric oxide in the blood vessels, which leads to vasodilation of the vessel, decreased platelet aggregation and decreased inflammation. Nitrous oxide is the same as laughing gas used by dentists!
- A 2008 study found that laughing could decrease both diastolic and systolic blood pressure. 200 individuals partook in laughter yoga for seven sessions over a three-week period saw a 6.18



percent decrease in systolic blood pressure and a 3.8 percent decrease in diastolic blood pressure. [69]

- In a 2001 study of 300 subjects with coronary heart disease (CHD) and controls found that that there is an inverse relationship between humor and CHD. Individuals with CHD are 40 percent less likely to laugh in routinely encountered situations of everyday life. [70]
- Watching a comedy movie that provoked laughter caused vasodilation in the brachial artery by 17 percent and 10 percent in the carotid artery compared to watching a documentary according

to a 2010 study with 17 healthy participants. This effect lasted for 24 hours after watching the comedy. [71]

Benefits of Laughter Yoga (science demonstrated that brain does not distinguish between forced and spontaneous laughter)

Physical Benefits:

- Boosts and strengthens the immune system.
- Oxygenates the body & increases stamina.
- Alleviates pain and gives a sense of wellbeing by releasing endorphins.
- Helps control high blood pressure and heart disease.
- Effective antidote for depression & anxiety- boosts serotonin levels.
- Gives an excellent internal massage to vital organs.
- Ensures good sleep and reduces snoring.
- Brings a happy glow to your face and makes your eyes shine.
- Laughing is a powerful form of exercise that gives you more of a cardiovascular workout than many "regular" aerobic activities.

Mental, Emotional & Spiritual Benefits:

- Laughter makes it easier to cope with life and its challenges.
- Laughter builds self-confidence.
- Laughter puts us intensely in the moment.
- Laughter allows people to be more open with each other.
- People who laugh don't worry as much as people who don't laugh.
- Laughter make us feel good because it defuses painful emotions by releasing them.
- Laughter lifts us up and makes life worth living.
- Laughter is an important social skill that keeps communications fun.
- Laughter interrupts the power struggle.
- When we laugh with others, criticism seems to collapse.
- Laughter breaks down the barriers between people and allows them to trust each other.
- Laughter Yoga aims to develop joyfulness, which is the unconditional commitment to have. Fun despite all of the possible problems that we are faced with in life.
- Laughter is a pathway to unconditional love.
- Laughter Yoga helps bring forth the best in human nature.

Life with Purpose

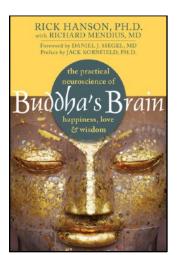
- Higher purpose in life may play an important role in protecting against myocardial infarction among older American adults with coronary heart disease. Prospective data from the Health and Retirement Study-a nationally representative panel study of American adults over the age of 50-were used. Analyses were conducted on the subset of 1,546 individuals who had coronary heart disease at baseline, adjusting for relevant sociodemographic, behavioral, biological, and psychological factors. Each purpose in life unit increase was associated 27 percent reduction in risk of heart attack. [72]
- Life with purpose also lead to significant reduction in risk of stroke (again after adjusting for all other known risk factors for stroke) In a study of 453 older participants (deceased of natural causes, who than underwent autopsy of the brain) demonstrated almost 50 percent less large brain infarcts among those who had compared to those who did not have a clear purpose in life. [73]

Resources (just a small sample!)

Books

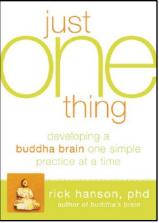
Buddha's Brain: The Practical Neuroscience of Happiness, Love & Wisdom, by Rick Hanson

This book connects Buddhist philosophy with neuroanatomy and is based on recent discoveries using functional MRI (fMRI). fMRI allows researcher to determine which part of the brain is activated depending on type of thoughts and emotions. It teaches us to recognize our thoughts and feelings and rather than acting them out become aware of them, recognize which part of the brain are they coming from and why.



Just One Thing: Developing a Buddha Brain One Simple Practice at a Time, by Rick Hanson

An abbreviated version of Buddha's Brain. Very simple and practical approach to neuroplasticity and how to rewire our brain within 3-6 months without all the information on brain function presented in the previous book. Read one chapter per week and practice!



Anger: Wisdom for Cooling the Flames Book by Thich Nhat Hanh

Very simple, practical and easy to follow approach how to deal with this most toxic emotion. Hint: Anger is not enemy! On personal note this book made a huge difference with my anger issues... (wm)

How God Changes Your Brain

Excellent book how faith based meditation rewires our brain

Are you overwhelmed? Do you procrastinate? Do you sometimes feel like you are your own worst enemy? Are you ignoring your dreams? Have you lost the courage to truly be yourself? Do you feel that your life lacks meaning and purpose? Do you find yourself avoiding the real issues in your life and focusing on the superficial?

Resisting Happiness Book by Matthew Kelly

Breaking through resistance, Kelly tells us, is essential to becoming thebest-version-of-ourselves and living with passion and purpose.

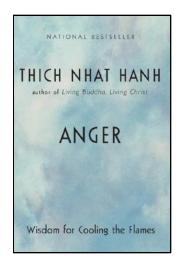
What is resistance? It's that sluggish feeling of not wanting to do something that you know is good for you. It's the inclination to do something that you unabashedly know is not good for you. It's the desire and tendency to delay something you should be doing right now.

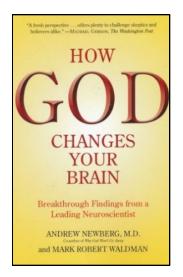
It is resistance that stands between you and happiness. In these pages, you will learn not only what it is, but how to recognize and conquer it in your own life.

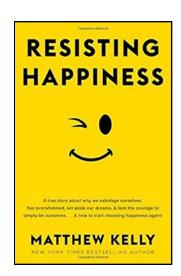
Review from: (https://dynamiccatholic.com/resisting-happiness-hardcover)

Websites

iRest.com - iRest Yoga Nidra Meditation, one of the principal programs offered by IRI, is a research-based transformative practice of deep relaxation and meditative inquiry, which is currently being utilized in VA hospitals, military bases, hospitals and clinics, hospice, homeless shelters, community programs, and schools.







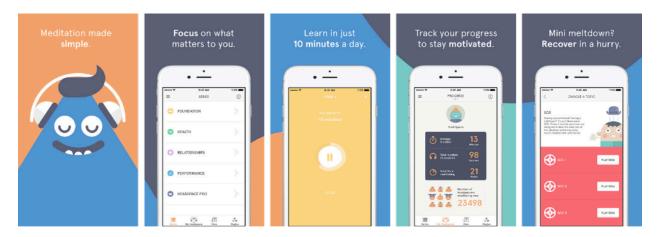
Research has shown that iRest effectively reduces PTSD, depression, anxiety, insomnia, chronic pain, and chemical dependency while increasing health, resiliency, and well-being.

Our favorite Apps

(paid versions tend to be better than the free one)

Headspace

Selected as one of the best medical apps.



Yoga Nidra

Is a simple technique of body awareness, no yoga stretches involved with an option between 15 and 45 minutes sessions. It is very effective for relaxation, depression, anxiety and insomnia. (similar to irest approach).



Calm

Is probably most comprehensive relaxation app on the market, with extensive options for various meditation sessions as well as techniques facilitating sleep.

There are many resources that will help you to become a happier person, choose what works for you!



References:

- 1. Publications, H.H., *Understanding the stress response Harvard Health*. Harvard Health Publications, 2016.
- 2. Mah, L., C. Szabuniewicz, and A.J. Fiocco, *Can anxiety damage the brain?* Curr Opin Psychiatry, 2016. **29**(1): p. 56-63.
- 3. Johansson, L., et al., *Midlife psychological stress and risk of dementia: a 35-year longitudinal population study.* Brain, 2010. **133**(8): p. 2217-2224.
- 4. Brunner, E., *Risk factors raised by socioeconomic deprivation that doctors can manage*, in *EAS Congress*. 2010: Hamburg, Germany.
- 5. Piletz, J.E., et al., *Pro-inflammatory biomakers in depression: treatment with venlafaxine*. World J Biol Psychiatry, 2009. **10**(4): p. 313-23.
- 6. Nabi, H., et al., *Effects of depressive symptoms and coronary heart disease and their interactive associations on mortality in middle-aged adults: the Whitehall II cohort study.* Heart, 2010. **96**(20): p. 1645-50.
- 7. Sokoreli, I., et al., *Depression as an independent prognostic factor for all-cause mortality after a hospital admission for worsening heart failure.* Int J Cardiol, 2016. **220**: p. 202-7.
- 8. Sherwood, A., et al., *Worsening depressive symptoms are associated with adverse clinical outcomes in patients with heart failure.* J Am Coll Cardiol, 2011. **57**(4): p. 418-23.
- 9. Vaccarino, V., et al., *Major depression and coronary flow reserve detected by positron emission tomography.* Arch Intern Med, 2009. **169**(18): p. 1668-76.
- 10. Roest, A.M., et al., *Anxiety and risk of incident coronary heart disease: a meta-analysis.* J Am Coll Cardiol, 2010. **56**(1): p. 38-46.
- 11. Hamer, M., G.J. Molloy, and E. Stamatakis, *Psychological distress as a risk factor for cardiovascular events: pathophysiological and behavioral mechanisms*. J Am Coll Cardiol, 2008. **52**(25): p. 2156-62.
- 12. Martens, E.J., et al., Scared to death? Generalized anxiety disorder and cardiovascular events in patients with stable coronary heart disease: The Heart and Soul Study. Arch Gen Psychiatry, 2010. 67(7): p. 750-8.
- 13. Lichtman, J.H., et al., Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. Circulation, 2014. **129**(12): p. 1350-69.
- 14. Towfighi, A., et al., *Poststroke Depression: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association.* Stroke, 2017. **48**(2): p. e30-e43.
- 15. Rollman, B.L., et al., *The Bypassing the Blues treatment protocol: stepped collaborative care for treating post-CABG depression.* Psychosom Med, 2009. **71**(2): p. 217-30.
- 16. Hare, D.L., et al., *Depression and cardiovascular disease: a clinical review.* Eur Heart J, 2014. **35**(21): p. 1365-72.
- 17. Doll, J.A., et al., *Participation in Cardiac Rehabilitation Programs Among Older Patients After Acute Myocardial Infarction*, in *JAMA Intern Med.* 2015: United States. p. 1700-2.
- 18. Blumenthal, J.A., et al., Enhancing Cardiac Rehabilitation With Stress Management Training: A Randomized, Clinical Efficacy Trial. Circulation, 2016. **133**(14): p. 1341-50.

- 19. Nabi, H., et al., *Increased risk of coronary heart disease among individuals reporting adverse impact of stress on their health: the Whitehall II prospective cohort study.* Eur Heart J, 2013. **34**(34): p. 2697-705.
- 20. Bot, I. and J. Kuiper, Stressed brain, stressed heart? Lancet, 2017. 389(10071): p. 770-771.
- 21. Rozanski, A., et al., *The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice.* JACC, 2005. **45**(5).
- 22. Lund, R., N.H. Rod, and U. Christensen, *Are negative aspects of social relations predictive of angina pectoris? A 6-year follow-up study of middle-aged Danish women and men.* J Epidemiol Community Health, 2012. **66**(4): p. 359-65.
- 23. Moller, J., et al., Work related stressful life events and the risk of myocardial infarction. Case-control and case-crossover analyses within the Stockholm heart epidemiology programme (SHEEP). J Epidemiol Community Health, 2005. **59**(1): p. 23-30.
- 24. Moreno-Smith, M., S.K. Lutgendorf, and A.K. Sood, *Impact of stress on cancer metastasis*. Future Oncol, 2010. **6**(12): p. 1863-81.
- 25. Roberts, A.L., et al., Association of trauma and posttraumatic stress disorder with incident systemic lupus erythematosus (SLE) in a longitudinal cohort of women. Arthritis Rheumatol, 2017.
- 26. Roberge, M.A., G. Dupuis, and A. Marchand, *Post-traumatic stress disorder following myocardial infarction: Prevalence and risk factors*, in *Can J Cardiol*. 2010. p. e170-5.
- 27. Edmondson, D., et al., *Posttraumatic stress due to an acute coronary syndrome increases risk of 42-month major adverse cardiac events and all-cause mortality.* J Psychiatr Res, 2011. **45**(12): p. 1621-6.
- 28. Sumner, J.A., et al., *Trauma Exposure and Posttraumatic Stress Disorder Symptoms Predict Onset of Cardiovascular Events in Women*. Circulation, 2015. **132**(4): p. 251-9.
- 29. Edmondson, D., et al., *Posttraumatic Stress Disorder and Risk for Coronary Heart Disease: A Meta-analytic Review.* Am Heart J, 2013. **166**(5).
- 30. Emdin, C.A., et al., *Meta-Analysis of Anxiety as a Risk Factor for Cardiovascular Disease*. Am J Cardiol, 2016. **118**(4): p. 511-9.
- 31. Cohen, B.E., et al., Association of cardiovascular risk factors with mental health diagnoses in Iraq and Afghanistan war veterans using VA health care. Jama, 2009. **302**(5): p. 489-92.
- 32. Brauser, D., *PTSD Linked to Increased Risk of Death, Cardiovascular Disease*. Medscape Medical News, 2010.
- 33. Mostofsky, E., E.A. Penner, and M.A. Mittleman, *Outbursts of anger as a trigger of acute cardiovascular events: a systematic review and meta-analysis*. Eur Heart J, 2014. **35**(21): p. 1404-10.
- 34. Arnold, S.V., J.A. Spertus, and B.K. Nallamothu, *The hostile heart: anger as a trigger for acute cardiovascular events*, in *Eur Heart J.* 2014: England. p. 1359-60.
- 35. Smyth, A., et al., *Physical Activity and Anger or Emotional Upset as Triggers of Acute Myocardial InfarctionClinical Perspective*. Circulation Research, 2016. **134**: p. 1059-1067.
- 36. O'Riordan, M., Anger and VT/VF. Medscape News, 2006.
- 37. Strike, P.C., et al., *Pathophysiological processes underlying emotional triggering of acute cardiac events*. Proc Natl Acad Sci U S A, 2006. **103**(11): p. 4322-7.

- 38. Metcalf, E., *Broken Heart Syndrome (Stress Cardiomyopathy) Symptoms, Causes, Treatments.* WebMD, 2011.
- 39. Ghadri, J.R., et al., *Happy heart syndrome: role of positive emotional stress in takotsubo syndrome.* European Heart Journal, 2016. **37**(37): p. 2823-2829.
- 40. YouTube. *Mayo Clinic talks broken heart syndrome YouTube*. 2014; Available from: https://www.youtube.com/watch?v=5f2Ga5O55k8.
- 41. Saposnik, G., et al., *Does a birthday predispose to vascular events?* Neurology, 2006. **67**(2): p. 300-4.
- 42. Denollet, J., A.A. Schiffer, and V. Spek, *A general propensity to psychological distress affects cardiovascular outcomes: evidence from research on the type D (distressed) personality profile.* Circ Cardiovasc Qual Outcomes, 2010. **3**(5): p. 546-57.
- 43. Ranjit, N., et al., *Psychosocial factors and inflammation in the multi-ethnic study of atherosclerosis*. Arch Intern Med, 2007. **167**(2): p. 174-81.
- 44. Fuller-Thomson, E., S. Brennenstuhl, and J. Frank, *The association between childhood physical abuse and heart disease in adulthood: findings from a representative community sample.* Child Abuse Negl, 2010. **34**(9): p. 689-98.
- 45. Carroll, D., et al., *Admissions for myocardial infarction and World Cup football: database survey.* Bmj, 2002. **325**(7378): p. 1439-42.
- 46. Leeka, J., B.G. Schwartz, and R.A. Kloner, *Sporting events affect spectators' cardiovascular mortality: it is not just a game.* Am J Med, 2010. **123**(11): p. 972-7.
- 47. Chan, C., et al., *Acute myocardial infarction and stress cardiomyopathy following the Christchurch earthquakes.* PLoS One, 2013. **8**(7): p. e68504.
- 48. Steinberg, J.S., et al., *Increased incidence of life-threatening ventricular arrhythmias in implantable defibrillator patients after the World Trade Center attack.* J Am Coll Cardiol, 2004. **44**(6): p. 1261-4.
- 49. Lan, C., et al., *Tai Chi training for patients with coronary heart disease*. Med Sport Sci, 2008. **52**: p. 182-94.
- 50. Yeh, G., *Tai Chi programs for patients with chronic heart failure*, in *Heart Failure Society of America Scientific Meeting*. 2010: San Diego, CA.
- 51. W, M.-B., *Yoga works for BP lowering in cardiac rehab*, in *Euro Prevent*. 2010: Prague, Czech Republic.
- 52. Lampert, R., et al., *Triggering of symptomatic atrial fibrillation by negative emotion*. J Am Coll Cardiol, 2014. **64**(14): p. 1533-4.
- 53. Nahab, F., et al., *Racial and geographic differences in fish consumption: the REGARDS study.* Neurology, 2011. **76**(2): p. 154-8.
- 54. Levine, G.N., et al., *Meditation and Cardiovascular Risk Reduction*. Journal of the American Heart Association, 2017.
- 55. Bhanoo, S.N., How Meditation May Change the Brain. Well, 2011.
- 56. Holzel, B.K., et al., *Mindfulness practice leads to increases in regional brain gray matter density.* Psychiatry Res, 2011. **191**(1): p. 36-43.
- 57. Paul-Labrador, M., et al., Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. Arch Intern Med, 2006. **166**(11): p. 1218-24.

- 58. Wisconsin, M.C.o., Transcendental Meditation helped heart disease patients lower cardiac disease risks by 50 percent. Science Daily, 2009.
- 59. Nidich, S.I., et al., A randomized controlled trial on effects of the Transcendental Meditation program on blood pressure, psychological distress, and coping in young adults. Am J Hypertens, 2009. **22**(12): p. 1326-31.
- 60. Schneider, R., et al., Abstract 1177: Effects of Stress Reduction on Clinical Events in African Americans With Coronary Heart Disease: A Randomized Controlled Trial. Circulation, 2009. 120(S461).
- 61. Slagter, H.A., et al., *Mental training affects distribution of limited brain resources*. PLoS Biol, 2007. **5**(6): p. e138.
- 62. Lutz, A., et al., Regulation of the neural circuitry of emotion by compassion meditation: effects of meditative expertise. PLoS One, 2008. **3**(3): p. e1897.
- 63. Yackle, K., et al., *Breathing control center neurons that promote arousal in mice*. Science, 2017. **355**(6332): p. 1411-1415.
- 64. Zeidan, F., et al., *Brain mechanisms supporting the modulation of pain by mindfulness meditation*. J Neurosci, 2011. **31**(14): p. 5540-8.
- 65. Jaskelioff, M., et al., *Telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice.* Nature, 2011. **469**(7328): p. 102-6.
- 66. Segal, Z.V., et al., *Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression*. Arch Gen Psychiatry, 2010. **67**(12): p. 1256-64.
- 67. Ornish, D., et al., Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study. Lancet Oncol, 2013. **14**(11): p. 1112-20.
- 68. Buric, I., et al., What Is the Molecular Signature of Mind-Body Interventions? A Systematic Review of Gene Expression Changes Induced by Meditation and Related Practices. Front Immunol, 2017. 8: p. 670.
- 69. Chaya MS, K.M., Nagendra R, et al., *The effects of hearty extended unconditional (HEU)* laughter using laughter yoga techniques on physiological, psychological, and immunological parameters in the workplace: a randomized control trial. , in American Society of Hypertension Annual Meeting. 2008: New Orleans, LA.
- 70. Clark, A., A. Seidler, and M. Miller, *Inverse association between sense of humor and coronary heart disease*, in *Int J Cardiol*. 2001: Netherlands. p. 87-8.
- 71. Sugawara, J., T. Tarumi, and H. Tanaka, *Effect of mirthful laughter on vascular function*. Am J Cardiol, 2010. **106**(6): p. 856-9.
- 72. Kim, E.S., et al., *Purpose in life and reduced risk of myocardial infarction among older U.S. adults with coronary heart disease: a two-year follow-up.* J Behav Med, 2013. **36**(2): p. 124-33.
- 73. Yu, L., et al., *Purpose in Life and Cerebral Infarcts in Community Dwelling Older Persons*. Stroke, 2015. **46**(4): p. 1071-6.

The Evolution of Obesity: Insights from the Mid-Miocene

Over 5 million years ago, global cooling that occurred in the middle Miocene rendered hominoids living in Europe at risk for starvation as seasonal climate change resulted in less availability of fruits during the winter months. During this time, a mutation in uricase occurred in early hominids that resulted in a rise in serum uric acid. Uric acid has been found to potentiate the effect of fructose to increase fat stores, suggesting that the mutation. [1]



Thank you, Grandpa, for your genes! I'll never be skinny again!

Study Shows Obesity Rate Exceed 10 Percent Worldwide

Global obesity problem now affects one in ten people in the world. An estimated 603 million adults are obese, including 107 million children. Excess weight accounted for four million deaths worldwide, 70 percent from cardiovascular disease, (reminder complications of diabetes, chronic renal failure, cancers and others). Almost 40 percent of those deaths were in people who were overweight, not obese. Obesity rates at least doubled in 73 countries between 1980 and 2015 and "continuously increased in most other countries. [2]



It is clear that obesity is generally the consequence of small, cumulative imbalances of energy intake and expenditure and once individuals who are obese and individuals who never were obese achieve their 'customary' body weights and composition, they tend to maintain and defend those weights by identical mechanisms.

There is a reason why there is no magic diet or pill...

Just eat less and exercise more?

Unfortunately, it is not as simple as calories in and calories out. Primates and humans in particular are extremely energy efficient. When compared to other animals such as red deer or seal, basal metabolic rate (BMR, amount of energy body uses at rest, to maintain function of vital organs) primates require only half of the energy! This is result of adaptation to constant cycles of feast (rapid accumulation of fat) and famine (slow use of the stored fuel to assure survival until more food is available).

Determinants of our metabolism

Genetics: "thrifty genes": humans who were able to rapidly gain weight and store it in fat, were more likely to survive prolonged periods of food shortage and as such were preferred by natural selection process.

Micorbiome: (see chapter 6) Depending on type of bacteria in our gut, absorption of nutrients will vary greatly (depending how complete is the digestion process).

Stress: in the past, main source of stress for human beings was lack of food. Nature equipped us with a survival mechanism in response to stress: reduce metabolism and increase appetite. Did you notice that when we are stressed out, everything tastes great?

In the same household, for individuals having the same type and amount of food, similar levels of activities BMR can vary by 500 kcal! This of course will result in weight gain in person with slower metabolism.

Are all calories created equal?

No, to digest some foods our body has to spend some energy first (for example almonds) this amount of energy is considerably less when we consume the same amount of almond butter! Think about the amount of chewing while eating almond versus almond butter! If we drink soda, loaded with sugar, it gets absorbed immediately without major expenditure by our body.

Glycemic Index (to look up GI of a food item check this link: (http://www.glycemicindex.com) [3]

- The **glycemic index** or (**GI**) is a number associated with a particular type of food that indicates the food's effect on a person's blood glucose (blood sugar) level.
- A value of 100 represents the standard, an equivalent amount of pure glucose.
- The Glycemic Index (GI) measures how quickly foods breakdown into sugar in our bloodstream. High glycemic foods turn into blood sugar very quickly. Starchy foods like potatoes are a good example. Potatoes have very high GI rating, it is almost the same as eating pure sugar!

Glycemic Index and Glycemic Load of Popular Foods Green = Low ~ Orange = Medium ~ Red = High				
Types of Food	Glycemic Index	Serving Size	Net Carbs	Glycemic Load
Peanuts	14	4 oz (113g)	15	2
Bean sprouts	25	1 cup (104g)	4	1
Grapefruit	25	1/2 large (166g)	11	3
Pizza	30	2 slices (260g)	42	13
Lowfat yogurt	33	1 cup (245g)	47	16
Apples	38	1 medium (138g)	16	6
Spaghetti	42	1 cup (140g)	38	16
Carrots	47	1 large (72g)	5	2
Oranges	48	1 medium (131g)	12	6
Bananas	52	1 large (136g)	27	14
Potato chips	54	4 oz (114g)	55	30
Snickers Bar	55	1 bar (113g)	64	35
Brown rice	55	1 cup (195g)	42	23
Honey	55	1 tbsp (21g)	17	9
Oatmeal	58	1 cup (234g)	21	12
Ice cream	61	1 cup (72g)	16	10
Macaroni and cheese	64	1 serving (166g)	47	30
Raisins	64	1 small box (43g)	32	20
White rice	64	1 cup (186g)	52	33
Sugar (sucrose)	68	1 tbsp (12g)	12	8
White bread	70	1 slice (30g)	14	10
Watermelon	72	1 cup (154g)	11	8
Popcorn	72	2 cups (16g)	10	7
Baked potato	85	1 medium (173g)	33	28
Glucose	100	(50g)	50	50
Nutritional values in this table is courtesy of: http://nutritiondata.self.com/topics/glycemic-index#ixzz2Jwaw2XZx				

Three ratings for GI:

In individual portions:

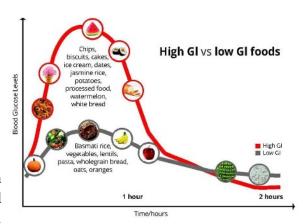
Low = GI value 55 or less

Medium = GI value of 56 - 69 inclusive

High = GI 70 or more

Glycemic load (GL)

• It measures the amount of carbohydrate in each serving of food. Foods with a glycemic load under 10 are good choices, these foods should be your first choice for carbs. Foods that fall between 10 and 20 on the glycemic load scale



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have a moderate effect on your blood sugar. Foods with a glycemic load above 20 will cause blood sugar and insulin spikes. Try to eat those foods sparingly.

What happens when we start dieting and exercising?

- Our body adapts to less food and more exercise, BMR declines. Our brain has a "thermostat" which controls weight.
- Imagine it is set at 200 lbs (which may not be the ideal weight) and you start losing weight, its going great, 10 lbs, then 20 lbs and you start marveling how easy it is, but then it stops. Weight is going up despite your efforts... What just has happened? Your brain just activated the thermostat, your body is concerned that you are



sick or starving (as you are eating less) and you are forging for food (your morning jogging). Your hunger increases, your body is not burning much fuel until you return to your starting weight. Sounds familiar?

The story of biggest losers: Can't win with Mother Nature!

- A 2016 study observed 14 biggest Loser participants at the end of their 30-week program and for 6 more years. The participants lost an average of 129 pounds during the program.
- In the 6 years following the show 13 participants regained weight and 5 were back at their original weight or higher.
- This may be due to the fact that the program severely affected their basal metabolic rate. It decreased an average of 610 kcal per day.

• Sadly, the metabolic rate damage still persisted after 6 years as the participants were burning 700kcal per day less than they were before starting the competition. [4]

Weight reset is a major driver of obesity.

According to a new scientific statement published by the Endocrine Society published June 26, 2017 in *Endocrine Reviews*, the body always tries to "defend" the level of body fat stores and then readjusts this "stable weight" at a higher level when a person gains excess weight. Obesity pathogenesis involves sustained positive energy balance (energy intake > energy expenditure) and resetting of the body weight 'set point' at an increased value." This "reset" may partly explain why it is so hard to lose excess weight and maintain this weight loss. Weight loss triggers biologic "defense response" attempting to bring weight to the last set point. [5]

Weight loss increases appetite over threefold!

In a recent weight loss study, for every kg of weight they lost, patients consumed an extra 100 calories a day more than three times what they would need to maintain the lower weight. Out of proportion increase in hunger is yet another mechanism our body defends itself against weight loss. [6]

Your gut bacteria are a part of the conspiracy....

Even gut bacteria (microbiome) as demonstrated in the below mice study are counteracting weight loss attempts. After a cycle of gaining and losing weight, mice metabolic function fully reverted to normal except the microbiome. For about six months after losing weight, post-obese mice retained an abnormal "obese" microbiome. This persistent microbiome accelerated the regaining of weight when the mice were put back on a high-calorie diet or ate regular food in excessive amounts. When bacteria were eliminated with broad-spectrum antibiotics, the exaggerated post-diet weight gain was eliminated. (Obviously we do not recommend antibiotics for weight loss but consider reprograming you gut microbiome as part of weighty loss program, (see chapter Human Microbiome) When formerly obese mice was implanted with gut microbes from mice that had never been obese it prevented excessive recurrent obesity. Next researchers supplemented post-dieting mice with flavonoids (here comes chocolate again!) added to their drinking water. This brought their flavonoid levels, and thus their energy expenditure, back to normal levels. As a result, even on return to a high-calorie diet, the mice did not experience accelerated weight gain.

Foods with a high flavonoid content include parsley, onions, blueberries and other berries, black tea, green tea and oolong tea, bananas, all citrus fruits, Ginkgo biloba, sea-buckthorns, and dark chocolate (with a cocoa content of 70% or greater).

Exercise and weight loss...

Exercise has many amazing benefits, listed in most of the chapters of the book. It includes maintenance of healthy weight. It is not a great tool for weight loss however. When you go for a long walk, what is the message your body is receiving? She is looking for food! Don't burn any fat until she finds it!

Why exercise is not working...

- We do not burn that many calories exercising (unless you are professional athlete like Michael Phelps). Machines and Fitbit often overestimate the amount of calories you burn sometimes as much as 25 percent. [7]
- On the way home, you stop at Starbucks to reward yourself for the 600 calories you burned (according to the machine) and the deficit is gone!
- Mounting evidence suggests that exercise makes us hungry and that we end up eating more extra calories in response to that hunger than we burn doing the exercise that made us hungry in the first place!

"You can't out-train a bad diet."

- Burning 300-600 calories on the stair climber or elliptical doesn't begin to "compensate" for supersized fries and a medium shake, nor even the most modest dish at Chipotle or Olive Garden.
- Yes, working out may allow you to "eat whatever you want" if whatever you want to eat is limited to meat and veggies. But if you think that hour in aerobics class bought you a free pass at the all-you-can-eat pasta station at the Bellagio buffet, you're delusional! (Adopted from article by Dr. Jonny Bowden published in Huffington Post 09/11/2012)
- Exercise does help to maintain weight in people who successfully lost weight.
- A study in the *Journal of the American Medical Association* followed the exercise habits of over 34,000 women and concluded that it took about an hour a day of moderate (3 mph walking) exercising to maintain weight.
- This research supports the findings of the National Weight Control Registry, which reports that 90 percent of people who have successfully lost weight and kept it off exercise on average for an hour a day. [7]

Water could help lose weight faster than diet drinks.

In a recent study, experts in diet and metabolism find that replacing low calorie 'diet' drinks with water can help increase the rate of weight loss in obese women with type 2 diabetes. 81 overweight and obese women with type 2 diabetes who were trying to lose weight to control their diabetes were recruited. They followed a hypo-energetic diet and their post-lunch drink option (diet drinks or water) for 24 weeks with the aim of losing 7-10 percent of their body weight at a rate of 0.5 to 1 kilogram a week. They also undertook a physical activity program, which gradually increased to achieve 60 minutes of moderate activity 5 days a week. For the post-lunch drink, these women were asked either to substitute water for diet drinks, or to continue drinking diet drinks. The result showed that women drinking water after their main meal at lunch time over 24 weeks lost on average 1.16kg more than the women who drank diet drinks after their meal. Moreover, women who drank water achieved a better improvement in insulin sensitivity. [8]

Breakfast is really a big deal!

A recent review of the dietary patterns of 50,000 adults who are Seventh Day Adventists over seven years clearly demonstrated that we should front-load our calories early in the day to jump-start our metabolisms and prevent obesity, starting with a big breakfast and tapering off to a smaller lunch and light supper (or no supper at all). Experiments in animals and trials in humans have pointed in the same direction,



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suggesting that watching the clock, and not just the calories, may play a more important role in weight control than previously acknowledged.

In 2017 American Heart Association (AHA) endorsed the principle that the timing of meals may help reduce risk factors for heart disease, like high blood pressure and high cholesterol. AHA, in their scientific statement emphasized that skipping breakfast (20 to 30 percent of American adults do it regularly) is linked to a higher risk of obesity and impaired glucose metabolism or diabetes. [9]

Skipping or skimming on breakfast leads to heart disease!

Cross-sectional analysis was performed within the PESA (Progression of Early Subclinical Atherosclerosis) study, a prospective cohort of asymptomatic (free of CV events at baseline) Lifestyle and multivascular imaging data along with clinical information were collected from 4,052 adults (without known heart disease) 40 to 54 years of age. Three patterns of breakfast consumption were studied: high-energy breakfast, when contributing to >20 percent of total daily energy intake (27% of the population); low-energy breakfast, when contributing between 5 percent and 20 percent of total daily energy intake (70% of the population); and skipping breakfast, when consuming <5 percent of total daily energy (3% of the population). People who ate less than 5 percent of their daily calories at breakfast were 2.5 times as likely to have generalized atherosclerosis (plaque buildup in the arteries) compared with those who ate the largest breakfasts. Meanwhile, those who had low-calorie breakfasts were at increased risk for early signs of plaque in their arteries, as well. [10]

Modest weight gain: lasting serious consequences

At the start of the study, more than 1,200 men and women, average age 44, who didn't have heart disease or even risk factors for heart disease, had MRI scans of their heart and several body fat measurements at baseline (beginning of the study) and 7 years later. The investigators found that people who increased their weight by as little as 5 percent were more likely to have thickening and enlargement of the left ventricle (the left lower chamber of the heart), which is an indicator of future heart failure. Ejection fraction (measure of mechanical performance of the left ventricle) decreased slightly as well. Changes were present independent of other risk factors affecting heart such as high blood pressure, diabetes, smoking.

Weight History Linked to Mortality

- A 2017 study published in the Annals of Internal Medicine found that individuals who have been over-weight or obese in the past have an increased risk of mortality compared to those who maintain a healthy body weight.
- The study, which included 225,000 participants, looked at a 16 year weight history and found that those with the lowest risk of mortality had a maximum BMI within normal range at all ages.



Those with a maximum BMI in the overweight, obese and obese 2 categories had an increased risk of death due to cardiovascular disease, cancer or respiratory disease. Hazard ratios were 1.06, 1.24 and 1.73 respectively. [11] People who lost weight, however, were more likely to have a decrease in the thickness of their heart muscle. The researchers also found that how

much someone weighed at the start of the study didn't have an effect on changes in their heart: even people of normal weight can damage their heart if they gain weight over time. [12]

Sleep and Weight

- A 2013 study found that insufficient amounts of sleep can lead to weight gain. 16 individuals were studied for about 14 days and during 5 of those days they were only allowed 5 hours of sleep.
- The study concluded that there was as increased total energy expenditure due the lack of sleep (higher amount of energy needed when our body is awaking) and with unrestricted access to food the participants compensated for this by in taking more calories, especially carbohydrates. This led to an average of a 2lb weight gain. [13]
- Another 2016 study including 12 healthy adults showed that when calories are restricted, just for 2 days we have longer deep sleep durations. In this study caloric intake was cut 10 percent for two days and deep sleep (stage 4) duration increased by 16.8 percent and total sleep duration by 21.7 percent. This effect was reversed when the participants could eat freely. [14]

Obesity Paradox

Obesity definitely leads to heart disease but being overweight and obese (but not extremely obese defined as > 100 lbs above ideal body weight) is associated with lower risk of complication related to bypass surgery of percutaneous coronary intervention (stent) as well as longer survival compared to normal weight or underweight patients undergoing the same procedures. Older heart attack patients who were mildly obese were 30 percent more likely to survive and spent fewer days in the hospital than those of normal weight or who were extremely obese. [15]

So, what to do? Take small steps...

Study Eat Smart, Move More, and Weigh Less (ESMMWL) use mindful eating techniques for effective weight loss.

• The study was a 15-week program including 80 participants, 42 of which followed and 38 that were assigned to the control group. The program promoted "eating fewer calories; including more fruits, vegetables, and whole grains in meals; eating breakfast regularly; controlling/decreasing portion sizes; eating more meals at



home; drinking fewer calorie-containing beverages; keeping a food/physical activity record; increasing physical activity; and watching less television."

- The participants lost an average of 4lbs compared to the control participants who lost an average of .6 lbs. This program was also successful in weight maintenance as ³/₄ of the participants kept the weight off or lost more.
- A 2016 study found that reducing risk of obesity can be as easy as replacing beer and soda with water!
- 15,765 non-obese adults were followed for 8.5 years and at the end of the study 873 participants became obese.
- Drinking a glass of water instead of beer or a sugar sweetened soft drink can decrease the risk of developing obesity by 20 and 15 percent respectively.
- A 2017 observational study including 16,000 individuals found that eating a vegetarian diet high in vegetable and fruit consumption can cut your risk for obesity greatly. Individuals were followed for ten years results found that those who were the most vegetarian saw a 43 percent decrease in the risk for developing obesity. [16]

Mindfulness

- Mindful eating has been shown to result in weight loss. [17]
- Watching TV or your phone leads to more calorie consumption!
- Focus on your food, be thankful for it and chew it slowly.

Takeru Kobayashi is a Japanese competitive eater. He holds many records, including eight Guinness Records, for eating hot dogs, meatballs, Twinkies, tacos, hamburgers, pizza, ice cream and pasta.

Gobbling Food May Boost Metabolic Risk

- After 5 years' follow-up of 1083 Japanese men and women who rated their eating speed during a yearly health exam, new-onset metabolic syndrome was diagnosed in 11.6 percent of fast eaters, 6.5 percent of normal eaters, and 2.3 percent of slow eaters.
- Fast eaters also saw greater gains in waist circumference (4.0 vs 1.5 vs 0.25 cm; and overall body weight (5.3 vs 0.23 vs -1.56 kg).
- If you chew your food many times, you spend more time at meals, you're more likely to feel full. It takes about 20 minutes for signals from your stomach indicating that you are full to reach your brain.



- Eating fast also causes acute glucose fluctuations. As a result, oxidative stress is increased, which leads to increased insulin resistance, decreased insulin secretion, and can further lead to hyperglycemia.
- At baseline, fast eaters were significantly more likely than normal or slow eaters to have higher levels of fasting blood glucose (104.0 vs 100.8 vs 98.3 mg/dL) and lower levels of HDL-cholesterol (56.8 vs 60.8 vs 62.6 mg/dL), though triglycerides and blood pressure were similar. [18]

Speed eating is not considered a form of exercise!

Yo-yo Dieting Dangerous to Health

- Yo-yo dieting is a term to describe those who repeatedly lose and regain weight.
- A 2017 study published in the New England Journal of Medicine followed 9,509 individuals with stable coronary artery disease for over five years and found remarkable results about weight fluctuations.
- The one-fifth of the group with the highest weight variability had a 78 percent higher risk of diabetes, a 117 percent higher risk of heart attack, a 136 percent higher risk of stroke, and a 124 percent higher risk of death! [19]
- Another study looking at 153,063 post-menopausal women found that yo-yo dieting for normal weight woman was associated with an increased risk for coronary artery disease by 65 percent and increased risk of cardiac death by 3.5 times.
- Over the 11 years the women were followed, there were 2,526 coronary heart disease deaths and 83 sudden cardiac death deaths. [20]

Practical approach to weight loss

- 1. Don't focus on it: your priorities are: be at peace, be active and it well. The more you get stressed out about your weight the slower your metabolism and bigger the hunger! You are so much better off to be happy and overweight as compared with skinny and angry!
- 2. Download one of the many apps for calorie counting such as MyFitnessPal or Lose It!
- 3. Purchase food scale and measuring cups.
- 4. Try to create menu ahead of time, selecting foods with low GI/GL.
- 5. Stick to the Mediterranean diet as much as you can. Eat at home.
- 6. Reprogram your gut bacteria: see chapter on Human Microbiome.



- 7. Set yourself a modest goal: no more than 1 lbs. per week.
- 8. Before going to a restaurant (if you must), check their menu on line and figure out the calorie count before you eat it.
- 9. Start regular exercise routine to maintain your weight loss. Subtract 20 percent from the number of calories burned displayed by the machine and/or Fitbit device before adding to total calorie count.
- 10. Practice mindful eating and recognize when you are really hungry versus want to eat from stress or boredom.
- 11. Get enough sleep.
- 12. Identify sources of stress and learn how to cope with it.
- 13. Have a bag of nuts with you, so you have something to snack on and you are not overwhelmed by hunger.
- 14. Don't stress out about weight creeping back up (metabolic reset): this just part of life, remember Mother Nature put many roadblocks to prevent us from losing weight, try again!

What happens to metabolism as we age?

Basal metabolic rate (BMR) is the energy expenditure of an individual after a 12- to 14-h overnight fast during a period of mental and physical rest in a thermoneutral environment (not to cold: shivering, not to hot: sweating) and reflects energy use of the body for such basic functions as maintenance of electrochemical gradients (generation of electric currents) transporting of molecules around the body, and biosynthetic processes.

Typically, BMR is the largest component of energy expenditure and comprises 50–70 percent of total expenditure in most adults. A decline in BMR with aging is well recognized is a sad fact of

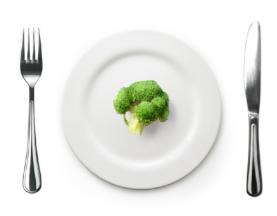
life. It drops around 2 percent per decade, staring at age of 25 (when we stop growing bone) Punchline: as we age, to maintain stable weight we have to eat less and if we become less active (burn less calories) which is the case for most of us, we have to eat even less! Does the hunger decrease as we age? Not mine! For example, if you are an active 154 lb 16-year-old you need 3200 kcal a day but when you turn into a sedentary 60-year-old to keep your weight you just need 2000 kcal: that's 1200 kcal less!



The difference in daily calorie intake between active 16-year-old and sedentary 60-year-old to maintain the same weight is equivalent to whole rotisserie chicken with skin! Sucks, doesn't it?

What are the consequences of very calorie restricted diets? (in addition to reducing your BMR)

If a person starts for example 900-calorie-a-day diet, body will have a hard time getting the required nutrients. Without the daily requirement of protein, body will break down won lean muscle mass. Basically, the body will make sure it gets what it needs to function and if it doesn't get what it needs from food, it will take what it needs from the muscles. It is pretty dumb, when you consider that you are in essence eating away at your own muscle mass, less lean muscle mass means you burn fewer calories



Mind over milkshakes: mindsets, not just nutrients, determine ghrelin response:

A rather unusual thing happens when you focus on making careful diet decisions. Even just thinking of your meal as a light choice, it can cause your brain to make more of the hormone ghrelin and more ghrelin makes you feel less full and signals your metabolism to slow down. To keep your ghrelin balanced, focus on the more indulgent parts of your meal such as nuts and cheese on your salad, rather than the lettuce. It also helps to pick foods that are both healthy and seem like a treat, like a warm bowl of soup with crusty whole-grain bread. [21]

Leptin

It lets your brain know how much fat is in your body. As leptin levels rise, your appetite diminishes. As leptin levels fall, your appetite increases. It regulates the rate of fat breakdown. As leptin levels rise, your metabolic rate increases. As leptin levels fall, your metabolism slows.

The body doesn't always listen to the leptin message known as leptin resistance. The leptin signal isn't being heard, so it cannot stimulate

LEPTIN & GHRELIN



your metabolism or suppress your appetite. Leptin resistance can make losing weight very hard. Leptin resistance can be caused by the typical modern lifestyle such as fast food, lack of physical activity, stress and sleep deprivation.

In a study of over 1000 volunteers, participants with short sleep had reduced leptin and elevated ghrelin. These differences in leptin and ghrelin lead to increase appetite, explaining the increased BMI observed with short sleep duration. In Western societies, where chronic sleep restriction is common and food is widely available, changes in appetite regulatory hormones with sleep curtailment may contribute to obesity. [22]

Ghrelin

Ghrelin is one of the main hormones to stimulate hunger. Ghrelin levels increase before meals and decrease after meals, it plays an important role in hunger and therefore weight gain.

Do you pay with plastic?

Some food items in grocery store that are commonly considered unhealthy (calorie dense) also tend to elicit impulsive responses. The pain of paying in cash can curb impulsive urges to purchase such unhealthy food products. Credit card payments, in contrast, are relatively painless and weaken impulse control. Consequently, consumers are more likely to buy unhealthy food products when they pay by credit card than when



they pay in cash. Analysis of actual shopping behavior of 1,000 households over a period of 6 months revealed that shopping baskets have a larger proportion of food items rated as impulsive and unhealthy when shoppers use credit or debit cards to pay for the purchases. When instructed to use cash, individuals selected healthier choices! [23]

DO YOU THINK ABOUT EXERCISE A LOT?

Just thinking about exercise can cause you to eat 50 percent more. Why? People assume that the upcoming workout gives them license to snack! [24]

Enhancing calorie Burning at work & HOME

The walls of your capillaries are lined with lipoprotein lipase, an enzyme that breaks down certain fats in the bloodstream. Sit for a few hours, and these enzymes start switching off. Sit all day, and their activity drops by 50 percent!

The "NEAT" Solution

Non-exercise activity thermogenesis (NEAT) is the energy that is used (calories burned) while engaging in everyday activities.

By adding small amounts of non-exercise-related activity to our daily routine we can increase metabolic activity of our body. Standing rather than sitting, increases energy expenditure threefold!

(Average sized person burns just five calories an hour while sitting and 15 while standing). Just by standing and stretching every hour one can boost metabolism by about 13 percent, fidget all day (tap your feet or bounce in your chair) and increase calorie burn by 54 percent: this may however be quite irritating to your coworkers! [25]

To Prevent Sitting At Home

The Danger Zones: TV and computer

Stand up and walk around (around, not to the refrigerator!). Try to this every time an advertisement comes on the TV.

Use stability ball. Sitting on a large, inflatable ball requires shifting slightly from side to side to keep balance engaging more abdominal and back muscles more than sitting in a regular chair. Strong abdominal muscles prevent back pain and enhance stability and balance.

Install exercise equipment treadmill, stationary bike, elliptical) near TV. Choose a half-hour show every day and exercise along it.

Place your computer on an elevated surface, such as a shelf or stand (to stand rather than sit in front of it).



Image source: http://ergonomicsguru.com

To Prevent Sitting At Work

Stand up and pace around when you answer the phone.

Talk to co-workers (which requires getting up and finding them) rather than sending emails or texts. Get up for 10 minutes every hour to stretch your back and legs while working on computer. You can take care of other tasks such as phone calls, which do not require sitting.

Use stairs. Avoid the elevator when going to and from your workplace.

Park your car a distance (half a mile, for example) from your office. If you take mass transit, get off the bus or subway one or two stops before your destination.

Use half your lunch hour for a walk.

Use a standing desk or treadmill desk.

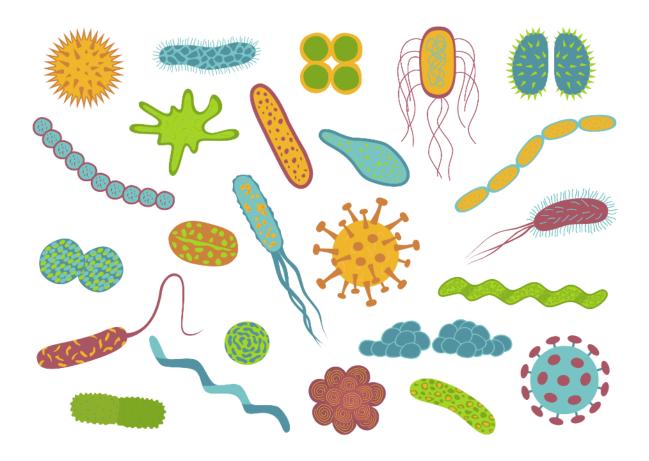
Source: Bottom Line/Health interview with James A. Levine, MD, PhD, director of the Non-Exercise Activity Thermogenesis (NEAT) Laboratory at the Mayo Clinic in Rochester, Minnesota. Coauthor of Move a Little, Lose a Lot (Crown).

References:

- 1. Chang, B.S., *Ancient insights into uric acid metabolism in primates*. Proc Natl Acad Sci U S A, 2014. **111**(10): p. 3657-8.
- 2. Afshin, A., et al., *Health Effects of Overweight and Obesity in 195 Countries over 25 Years*. N Engl J Med, 2017. **377**(1): p. 13-27.
- 3. Sydney, T.U.o. *Glycemic Index*. 2017; Available from: http://www.glycemicindex.com/.
- 4. Fothergill, E., et al., *Persistent metabolic adaptation 6 years after "The Biggest Loser" competition.* Obesity (Silver Spring), 2016. **24**(8): p. 1612-9.
- 5. Schwartz, M.W., et al., *Obesity Pathogenesis: An Endocrine Society Scientific Statement*. Endocrine Reviews, 2017. **38**(4): p. 267-296.
- 6. Polidori, D., et al., *How Strongly Does Appetite Counter Weight Loss? Quantification of the Feedback Control of Human Energy Intake*. Obesity (Silver Spring), 2016. **24**(11): p. 2289-2295.
- 7. Lee, J.M., Y. Kim, and G.J. Welk, *Validity of consumer-based physical activity monitors*. Med Sci Sports Exerc, 2014. **46**(9): p. 1840-8.
- 8. Madjd, A., et al., Beneficial effects of replacing diet beverages with water on type 2 diabetic obese women following a hypo-energetic diet: A randomized, 24-week clinical trial. Diabetes Obes Metab, 2017. **19**(1): p. 125-132.
- 9. St-Onge, M.P., et al., *Meal Timing and Frequency: Implications for Cardiovascular Disease Prevention: A Scientific Statement From the American Heart Association*. Circulation, 2017. **135**(9): p. e96-e121.
- 10. Uzhova, I., et al., *The Importance of Breakfast in Atherosclerosis Disease*. JACC, 2017. **70**(15).
- 11. Yu, E., et al., Weight History and All-Cause and Cause-Specific Mortality in Three Prospective Cohort Studies. Annals of Internal Medicine, 2017. **166**(9): p. 613-620.
- 12. Wilner, B., et al., *Dynamic Relation of Changes in Weight and Indices of Fat Distribution With Cardiac Structure and Function: The Dallas Heart Study.* J Am Heart Assoc, 2017. **6**(7).
- 13. Markwald, R.R., et al., *Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain.* Proc Natl Acad Sci U S A, 2013. **110**(14): p. 5695-700.
- 14. Collet, T.H., et al., *The Sleep/Wake Cycle is Directly Modulated by Changes in Energy Balance*. Sleep, 2016. **39**(9): p. 1691-700.
- 15. Holroyd, E.W., et al., *The Relationship of Body Mass Index to Percutaneous Coronary Intervention Outcomes: Does the Obesity Paradox Exist in Contemporary Percutaneous Coronary Intervention Cohorts? Insights From the British Cardiovascular Intervention Society Registry.* JACC Cardiovasc Interv, 2017. **10**(13): p. 1283-1292.
- 16. Daily, S., *Eating a diet rich in fruit and vegetables could cut obesity risk*. Science News, 2017.
- 17. Ruffault, A., et al., *The effects of mindfulness training on weight-loss and health-related behaviours in adults with overweight and obesity: A systematic review and meta-analysis.* Obes Res Clin Pract, 2016.
- 18. Yamaji, T., et al., Abstract 20249: Slow Down, You Eat Too Fast: Fast Eating Associate With Obesity and Future Prevalence of Metabolic Syndrome. Circulation, 2017. 136:A20249.

- 19. Bangalore, S., et al., *Body-Weight Fluctuations and Outcomes in Coronary Disease*. New England Journal of Medicine, 2017. **376**: p. 1332-1340.
- 20. Rasla, S., *Yo-yo dieting dangerous even if you're not overweight*, in *American Heart Association*. 2017, @EurekAlert: New Orleans, LA.
- 21. Barański, M., et al., *Effects of organic food consumption on human health; the jury is still out!* Food Nutr Res, 2017. **61**(1).
- 22. Taheri, S., et al., Short Sleep Duration Is Associated with Reduced Leptin, Elevated Ghrelin, and Increased Body Mass Index. PLoS Med, 2004. 1(3).
- 23. Thomas, M., K.K. Desai, and S. Seenivasan, *How Credit Card Payments Increase Unhealthy Food Purchases: Visceral Regulation of Vices.* Journal of Consumer Research, 2017. **38**(1): p. 126-139.
- 24. Hamilton, M.T., et al., *Too Little Exercise and Too Much Sitting: Inactivity Physiology and the Need for New Recommendations on Sedentary Behavior.* Curr Cardiovasc Risk Rep, 2008. **2**(4): p. 292-8.
- 25. Levine, J.A., S.J. Schleusner, and M.D. Jensen, *Energy expenditure of nonexercise activity*. Am J Clinical Nutr, 2000. **72**: p. 1451-1454.

The Human Microbiome



Our bodies contain about 1000 species of bacteria and 39 trillion bacteria cells and live most prominently in our intestines. There are 30 trillion cells in our body. [1]

- Most of these microbes are commensals (relationship in which one species is benefited while the other is unaffected) and mutualists (relationship between species of organisms in which both benefit from the association) while a small amount are pathogens (bad guys). Microbiome directly affects many aspects of our health.
- Probiotics reside in the entire digestive tract from mouth to the rectum.
- The human body contains around 3 pounds of probiotic organisms, which is the same weight as brain.
- If the bacteria in your gut were connected end to end, it would encircle Earth 2.5 times. (over 62000 miles!)
- There are over 1000 probiotic strains (types of bacteria) in human body but every individual has their own unique makeup.
- Probiotics facilitate absorption of minerals and micronutrients, such as copper, calcium, magnesium, iron, manganese, potassium, and zinc.

- The digestive system is often called the "second brain" because the vagus nerve sends information from the gut to the central nervous system.
- The gut contains over 100 million neurons (nerve cells) and produces up to 90 percent of the body's serotonin.
- Probiotics affect emotions, mood, quality of sleep, resilience to stress via their effect on neurotransmitters.
- High fructose corn syrup, alcohol, western diet, mental stress, antibiotics (either lack of sleep, lack of exercise all reduce not only the total number but number of species of beneficial bacteria. As there is no vacuum in the gut, probiotic bacteria are replaced than with evil ones.

They are friends not enemies (most of the time)



And the 5 second rule...



Befriend them early!

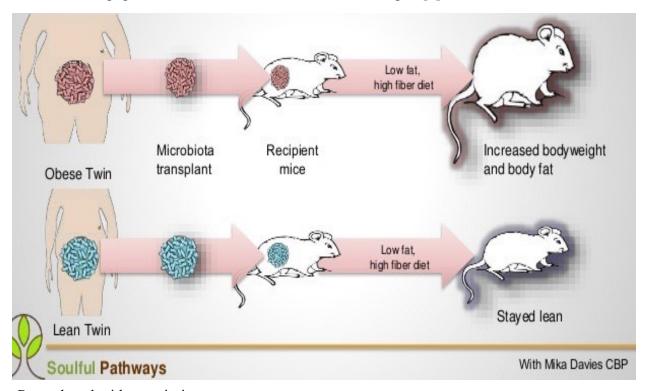
Human Microbiome and the Heart

A 2015 study looked at 839 participants' genome, gut microbiome, blood lipid levels and BMI (body mass index). Results found 34 microbes species that were associated with BMI and lipid levels. Higher microbe diversity is linked to HDL levels. 4.5 percent of the variance in BMI, 6 percent in triglycerides, and 4 percent in HDL can be explained by the microbiota when independent from age, gender and genetic factors. [2]

Can Microbes Cause Weight Gain?

The answer is yes! When feces are transferred from normal, obese and underweight mice to newborn mice, animals adopt the phenotype! Of course, your frequent trips to Golden Coral did not help either...

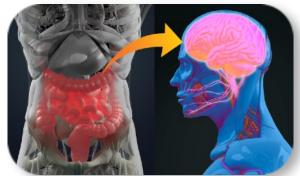
One study including twins, one obese and one lean, and germ-free mice found that when the mice were populated with bacteria from the obese twin's gut the mice became fatter than the mice who was populated with bacteria from the lean twin's gut. [3]



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Gut Microbes and the Brain

- The gut microbiome had been called the "second brain" as it can send signals and influence brain development, mood and behavior in humans.
- Neurochemicals and neurotransmitters are released from the gut and communicate with the brain.
- The gut produces the neurotransmitter, serotonin, which is known as the "happy hormone" and also serves as important regulatory factor in the GI tract. [4]



- A 2004 study found that mice without microbes had an increased level of corticosterone, a stress hormone in the hypothalamus, which causes them to display an elevated response to restraint stress compared to mice with diverse microbes. [5]
- A 2014 study showed that mice given bacterium B. Longum and B. Breve saw decreased levels of anxiety that were similar to taking the anti-anxiety medication, escitalopram. [6]
- B. infantis had also been seen to decrease depressed behaviors in mice and is similar to treatment with antidepressant medications. [7]
- Two 2011 and 2015 studies using humans as subjects found that consuming probiotic fermented milk can actually decrease feelings of sadness and anxiety levels. This proves that the gut microbes not only affect animals but also control human emotional stimuli. [8], [9]

Craving Control

- When we consume food, gut hormones send signals to the brain through the vagus nerve to control food consumption. Microbes living in the gut are responsible for manipulating eating behavior. The microbes send signals through the gut-brain axis and change taste receptors to influence what we intake on their behalf to thrive. The nutrients they microbes cause us to crave may be good or bad on our health. [10]
- A 2007 study found that those who craved chocolate had different microbe metabolites than those without cravings! [11]

Prebiotics in diet improve sleep, buffer impacts of stress

Dietary prebiotics can improve non-REM sleep, as well as REM sleep after a stressful event. When beneficial bacteria digest prebiotic fiber, they not only multiply, improving overall gut health, but they also release metabolic byproducts which can influence brain function. In an animal study, scientists discovered that rats on the prebiotic diet spent more time in non-rapid-eye-movement (NREM) sleep, which is restful and restorative, than those on the non-prebiotic

diet. After being exposed to a stressor, the rats on the prebiotic diet also spent more time in rapid-eye-movement (REM) sleep. REM sleep is believed to be critical for promoting recovery from stress, with research showing that those who get more REM sleep post-trauma are less likely to suffer from post-traumatic stress disorder. Stress has previously been shown to reduce healthy diversity of gut bacteria and to lead to a temporary flattening of natural fluctuations in body temperature. But rats on the prebiotic diet were buffered from these impacts, maintaining a healthy and diverse gut microbiota and normal temperature fluctuations even after stress exposure. [12]



Parkinson's disease starts in the gut

Researchers used mice genetically programmed to develop Parkinson's as they produced very high levels of the protein alpha-synuclein, which is associated with damage in the brains of Parkinson's patients. But only those animals with bacteria in their stomachs developed symptoms. Sterile mice remained healthy. Further tests showed transplanting bacteria from Parkinson's patients to mice led to more symptoms than bacteria taken from healthy people. Researchers clearly established that that gut bacteria regulate, and are even required for, the symptoms of Parkinson's disease! [13]

What to Feed Your Gut

- Probiotics: fermented foods already containing beneficial bacteria and
- Prebiotic foods: which will be fermented in the gut.

(Think: probiotics are the settlers, prebiotics is the settlement, settlers can't survive without settlement)

Keep in mind that most of the bacteria in fermented foods and in probiotic capsules will be destroyed in stomach by hydrochloric acid as such probiotic supplements or food will not be sufficient without the prebiotics to sustain the bacteria in the gut!

Examples of probiotic food:

- Yogurt. Not all yogurts are equal, choose lowest sugar content and of course non-pasteurized!)
- Kombucha tea (fermented tea)
- Miso soup
- Fermented soy beans
- Kefir
- Sauerkraut, Kimchi
- Dark chocolate. (it is both, probiotic and prebiotic)

Probiotic foods examples:

Kimchi



Miso soup



Sauerkraut



Kombucha: fermented tea



Tempeh: fermented soy beans



Poi: traditional Hawaiian dish made from fermented taro root



Kefir and Yoghurt



Examples of prebiotic foods:

- Acacia gum (or Arabic gum)
- Raw chicory root (powder available)
- Raw Jerusalem artichoke (powder available)
- Raw dandelion greens
- Raw garlic
- Raw leeks



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The Human Microbiome

Examples of prebiotic foods								
Prebiotic	Fiber by weight	Amour	nt of Daily Serving					
Raw Chicory Root	64.6%	9.3 g	1/3 oz.					
Jerusalem Artichoke	31.5%	19 g	³ / ₄ OZ.					
Raw Dandelion Greens	24.3%	24.7 g	1 oz.					
Raw Garlic	17.5%	34.3 g	1.2 oz.					
Raw Leeks	11.7%	51.3 g	1.8 oz.					
Raw Onion	8.6%	69.8 g	2.5 oz.					
Cooked onions	5%	120 g	1/4 lb.					
Raw Asparagus	5%	120 g	1/4 lb.					
Raw Banana	1%	600 g	1.3 lbs.					
Source: https://www.prebiotin.com/foods-containing-prebiotics/								

Source: https://www.prebiotin.com/foods-containing-prebiotics/

Authors comment: It is not easy (yes, I did try) to eat the quantities of prebiotics recommended above. There are supplements available such as chicory root powder, Jerusalem artichoke powder etc, which can easily be added to food. All of course, available on Amazon.

Trivia: why onions makes us cry?

Onions are vegetables that grow underground, and beneath the surface are a lot of animals who are trying to grab a bite to eat, but onions have a way to defend themselves.

Sulfur in the soil is absorbed by growing onion and creates amino acid sulfoxides, which are sulfur compounds that readily turn into a gas. When an onion is injured (bite, knife etc), the sulfoxides and onion enzymes are released, and this creates sulfenic acid. The sulfenic acid and onion enzymes react and create a noxiuous gas with a long name: syn-propanethial-S-oxid. This gas floats up from the chopped or bitten onion and deters critters and causes humans to shed tears! [14]

Reprograming your gut: The Gut Makeover Diet

First 2 weeks

- Eat three main meals per day, no snacks between.
- 12-hour overnight fast between dinner & breakfast, with just water permitted between.
- Eat seven cups of plants (uncooked volume) per day (five as vegetables, two as fruit).
- Eat protein with each meal: poultry, fish, eggs (Do not eat eggs 7 days a week as it will lead to production of TMAO, 4-5x a week is ok), nuts, or seeds.
- Eat between 20 and 30 different types of plants (fresh herbs, vegetables, and fruits) over the course of a week for variety.
- Use extra virgin olive oil for salad dressing cooking (but no frying).
- Chew food thoroughly–at least 20 chews per mouthful.
- Eat as much as you please: do not restrict calories.

In the second half of the plan (weeks 2–4) participants also:

- Can eat butter and ghee (filtered butter).
- Consume probiotic foods such as fermented milk kefir, sauerkraut, tempeh, and miso.
- Increase their intake of prebiotic vegetables such as bananas (preferably still green) fennel, asparagus, cold potatoes, onions, garlic, leeks, fennel, Jerusalem artichokes, pak choy (also known as bok chi, type of Chinese cabbage).
- Consume bone broth/stock.

Excluded from the diet throughout the four weeks:

- Refined sugars.
- Grains (e.g. wheat, rice, oats, maize, quinoa) and pulses (e.g. lentils and beans) but ok to reintroduce later.
- · Alcohol.
- · Caffeine.
- Dairy (first 2 weeks just fermented then ok to reintroduce)
- After those 4 weeks continue with Mediterranean diet, which by itself is rich in prebiotic foods.

The above intervention, designed to manipulate gut bacteria was tested in a small group of 21 healthy volunteers and had a significant impact on digestion, reducing IBS (irritable bowel syndrome) type symptoms. There was also a striking reduction in negative symptoms related to cognition, memory and emotional wellbeing, including symptoms of anxiety and depression. Dietary gut microbiome manipulations have the power to exert positive physical and psychological health benefits! [16] (Adopted and modified from: Hyde J. The Gut Makeover. London: Quercus Editions Ltd; 2015.) [15]

Probiotic supplements: Do they really work?

Should I take probiotic pills?

No. You should not take probiotics, unless recommended or prescribed by physician.

What are the downsides to taking probiotics?

Probiotics are not regulated by the US Food and Drug Administration (the FDA) the way standard medicines are. That means that the companies that package probiotics don't have to prove that the ingredients listed on the label are actually in the bottle. In the end, you could buy a bottle that does not have what you think it has, so you could lose money. (Some probiotic pills are quite expensive!)

The U.S. Food and Drug Administration (FDA) has not approved any probiotics for preventing or treating any health problem.

There are medical indications for probiotics use such as inflammatory bowel disease, irritable bowel and clostridium dificile infections.

Examples of medically used probiotics, some of the more commonly available probiotics include:

- VSL#3 (Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, Streptococcus thermophilus)
- Align (B. infantis)
- Culturelle (L. rhamnosus GG)
- DanActive (L. casei)
- Mutaflor (E. coli Nissle 1917)
- Florastor (S. boulardii)

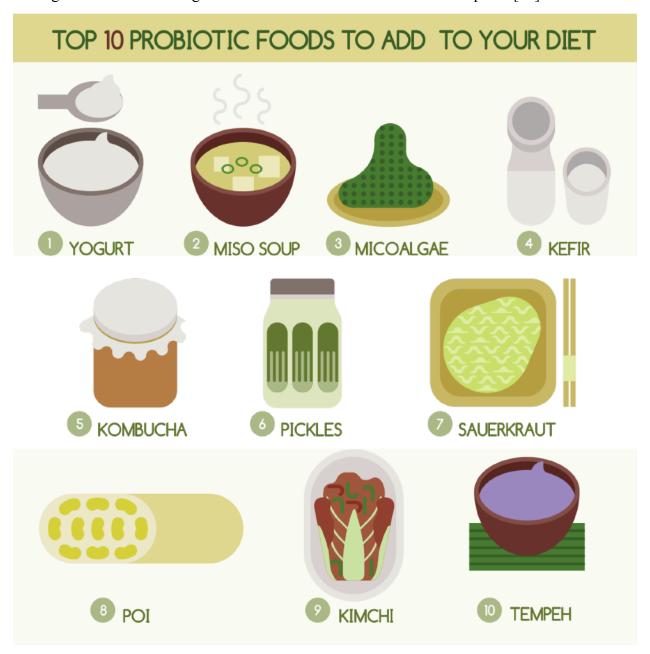
(Source uptodate.com)

About VSL#3

VSL#3 is a high potency probiotic medical food designated for the dietary management of ulcerative colitis, irritable bowel syndrome and. It is a medical food and must not be confused with an over-the-counter dietary supplement. It requires prescription and is dispensed by a pharmacist. VSL#3 is 10 times more potent than the average probiotic (average CFU = 15.5 billion) – The average probiotic contains about 4.3 billion CFU. (CFU stands for colony forming unit, which essentially stands for number of living bacteria in a preparation) VSL#3 formulations contain from 225 billion to 900 billion bacteria per serving (available by prescription). VSL#3 is one of the most potent probiotics in the world. (Source: www.vsl3.com)

Mechanisms of benefit of probiotics supplements in the digestive tract

- Suppression of growth or epithelial binding/invasion by pathogenic bacteria [17]
- Improvement of intestinal barrier function [18]
- Modulation of the immune system. Several probiotic species or their products induce protective cytokines, including IL-10 and TGF-beta, and suppress proinflammatory cytokines, such as TNF, in the mucosa of patients with ulcerative colitis, and Crohn disease [19]
- Modulation of pain perception in the gut. Some Lactobacillus strains appear to induce expression of micro-opioid and cannabinoid receptors in intestinal epithelial cells and mediate analgesic functions in the gut in a manner similar to the effects of morphine [20]



• Research has shown that diet changes can change our gut bacteria within three to five days. Participants who ate an animal-based diet had increases in bile-tolerant bacteria while plant-based diets increase bacteria that promote the breakdown of carbohydrates. [21]

And of course, do not forget chocolate which is both probiotic (chocolate beans were fermented in the process) and prebiotic!

Cocoa powder is packed with potent antioxidants: polyphenols. There is one major problem with many polyphenols: They are too large to get absorbed into the blood. Gut microbes break down the polyphenols into smaller molecules that are more likely to make it across the gut into the blood. In addition, microbes break down the fiber in the chocolate into short fatty chain acids, which get absorbed and can have an effect on satiety. [22]

Yogurt and depression

• Women consuming a serving of whole fat yogurt were 34 percent less likely to be depressed compared to women who consumed less than a serving a week. Eating low fat yogurt was linked to higher rate of depression. [23]

Yogurt and immune system

• Daily consumption of dairy yogurt containing L. paracasei, B. lactis and heat-treated L. plantarum significantly improved immune function by enhancing NK cell (natural killer cells, fighting cancer and bacterial infection) function and IFN-γ concentration (interferon gamma). [24]

Tryptophan in turkey and cheese may is good for our gut!

Commonly associated with turkey, the amino acid tryptophan is found in lots of protein-rich foods, like dairy, nuts, and beans. Immune cells patrol the gut to make sure harmful microbes hidden in the food we eat don't sneak into the bod. Cells that are capable of triggering inflammation are balanced by cells that promote tolerance, protecting the body without damaging sensitive tissues. But when the balance tilts too far in the wrong direction, inflammatory bowel disease can be the result.

Researchers have discovered that a kind of tolerance-promoting immune cell appears in mice that carry a specific bacterium in their guts. The bacterium needs tryptophan (an amino acid, a building block of protein) to survive. The more of this specific bacterium (Lactobacillus reuteri count in the gut, the more tolerance promoting cells were present! If those findings are confirmed in people, it would suggest that the combination of L. reuteri and a tryptophan-rich diet may foster a more tolerant, less inflammatory gut environment, which could mean relief for the million or more Americans suffering with inflammatory bowel disease. [25]

Walnuts improve gut health.

In an animal study walnuts increased the abundance of Firmicutes and reduced the abundance of Bacteriodetes. Walnuts enriched the microbiota for probiotic-type bacteria including Lactobacillus, Ruminococcaceae, and Roseburia while significantly reducing Bacteroides and Anaerotruncus. (The bad guys!). Walnut consumption altered the gut microbial community suggesting a new mechanism by which walnuts may confer their beneficial health effects. [26]

Fish, Omega-3 and your gut.

Group of British scientist analyzed data collected from 876 middle-aged and elderly female twins (average age 65) who'd previously been studied to look for links between their genetic profiles and gut microbiomes as they relate to weight gain and disease. Study concluded that higher blood levels of omega-3s (especially DHA) and higher dietary intakes of omega-3s were linked to healthier, more diverse microbiome, specifically by higher levels of friendly bacteria called Lachnospiraceaes. High omega-3 blood levels to high fecal levels of NCG (N-carbamylglutamate) a compound that exerts antioxidant effects in the gut, and is likely to reduce inflammation. [27]

Whether a diet works might depend on which bacteria are in your gut.

Using fecal samples, researchers analyzed the ratio of two gut bacteria, Prevotella and Bacteroides, in 62 overweight people. For 26 weeks, participants were randomly assigned to a low-fat diet high in fiber, fruits, vegetables and whole grains (named New Nordic Diet) or just a standard diet called Average Danish Diet. (Since the study was performed in Denmark)

Those on the high-fiber diet with a high Prevotella to Bacteroides ratio lost an average of 10 pounds of body fat, three and a half pounds more than those on the diet with a low ratio. Those on the regular diet with a high Prevotella ratio lost four pounds, compared with five and a half pounds for those with a low Prevotella ratio, a statistically insignificant difference. [28]

Gut Bacteria

Fluctuates with the Seasons.

Hadza is a small nomadic community of 1300 in Tanzania live solely on the animals they kill, along with honey, berries and a few other wild foods which used to be our original way of life. Researchers discovered that Hadza gut microbiome predictably changes from season to season. Some bacterial species disappear entirely and then return, in a rhythm that likely reflects regular changes in the Hadza diet. Many gut bacteria that wax and wane drastically are rare in people living in industrialized societies. As more societies switch to a Western diet, their microbiomes changes, altering their health!

The Hadza hosted a much greater diversity of gut microbial species than did the Italians, the researchers found, and there were some fundamental differences in species they carried. Some that were common in the Hadza were rare or missing from the Italians.

Hadza dictates the composition of these bacterial communities. Throughout the year, the Hadza gather fruits from baobab trees, but in the dry season, they also dig for tubers and eat lots of meat, because it is easier to hunt for animals on a parched landscape. In the wet season, they forage for berries and harvest honey from beehives.

In this study scientists compared the Hadza microbiome with those of people in 17 other societies, including urban Americans and Yanomamo villagers in the Amazon rain forest.

The Hadza microbiome is most similar to those in traditional societies, and least to the industrialized ones. The researchers found that the species that set the Hadza apart from industrial societies the most are also the ones that are the most seasonal.

The families of bacterial species that swing most strongly over a year in the Hadza gut are extremely rare in developed countries.

The Hadza may offer clues about what the microbiome was like in other societies before diets were transformed by modern agriculture and industry. Refined sugar and other new foods, favors a new set of gut microbes over ones that fed on tough plant fibers, and once people began eating the same foods year-round, a loss of seasonality may have meant that some ancestral bacterial species were lost: it is possible that this change resulted in chronic inflammation and diseases of modern society as as hypertension, diabetes and heart disease

Researchers found that microbes in the guts of Americans make more enzymes that degrade mucins (protective carbohydrates produced in the mucus lining of the intestines) compared with those in the Hadza. These enzymes allow bacteria to harvest carbohydrates from the mucosal lining of the gut, rather than from plant fiber. This means that you bacteria, instead of feeding on fiber feeds on you! [29]

Unhealthy gut microbes might be a cause of high blood pressure.

Scientist reported a significant increase in the Firmicutes:Bacteroidetes ratio in the hypertensive rates, as compared to the normotensive rats. Animals from both group were treated with antibiotics to kill their own bacteria. When normotensive rate received pellets containing feces of hypertensive rats, their systolic blood pressure jumped by 26 mm Hg and when hypertensive rats received pellets with feces of normotensive rat, their blood pressure was reduced (to a smaller extent). Gut dysbiosis (imbalance between good and bad bacteria) can directly affect SBP. Manipulation of the gut microbiota may represent an innovative treatment for hypertension. [30]

Authors comment: Please do not try it at home. It is difficult for you to figure out which of your rats have high blood pressure and which have not!

Diabetes linked to bacteria invading the colon.

Gut microbiota that live in the outer regions of the mucus and remain a safe distance from epithelial cells (inner lining of the gut) provide a benefit to the host, but that microbiota that encroach upon host cells drive chronic inflammation that interferes with the normal action of insulin, promoting type 2 diabetes. In a clinical study, investigators measured this distance between bacteria and epithelial cells in individuals undergoing colonoscopy. Researchers discovered the shorter bacterial-epithelial distance the higher body mass index, fasting blood sugar and hemoglobin A1C (which is a measure of chronic blood sugar control). [31]

Fecal transplant anyone?

• Bacterial flora can be changed within 24 hours. A potentially life-threatening infection can be treated through fecal-derived microbiota transplantation. This is becoming a common practice when infection does not respond to standard antibiotic therapy. Purified feces of a healthy donor are administered during colonoscopy or enema. Most recent research demonstrated feasibility of fecal transplant using a multilayer acid resistant capsule. [32]



Check out Fecal bank! (www.openbiome.org)

Consider becoming a fecal donor! The vetting is so rigorous only about 3 percent of applicants are accepted. And once you pass, ideally you will donate every day. Donors received \$ 40 per poop! One donation will provide cure for 8 patients with clostridium dificile infection, which affect 500,000 Americans a year and is responsible for 14,000 deaths a year!

Alcohol and Our Gut

- Excessive alcohol consumption can cause changes in the type of gut flora (more bad guys!).
- Alcohol abuse can lead to small intestine bacteria overgrowth and dysbiosis (microbe imbalance or maladaptation). Increased gut permeability leads to the translocation of bacterial products into the liver portal blood leading to inflammation and fibrosis causing liver disease.



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• Research has shown that prebiotics, probiotics and synbiotics (combination of prebiotics and probiotics) are capable of improving liver function or preventing liver damage in individuals with alcohol abuse and liver damage. [33]



Gut Microbe Diversity and Exercise

Exercise can have a positive effect on our gut health!

- A 2014 study including 63 participants, 40 elite professional rugby players and 23 controls, found that athletes and controls had significantly different microbe diversity and plasma creatine kinase and inflammatory and metabolic markers. The athletes had gut bacteria that represented 22 phyla. (Species)
- The athletes were found to have increased levels of Akkermansiaceae, bacteria that has been linked in past studies with a decreased risk for obesity.



• Increased gut diversity was linked to increased protein consumption. [34]

Do you want to learn about your own gut microbiome?

Cost of microbiome analysis (including DNA sequencing) is dropping, starting at \$89 and may be covered by insurance.

There are multiple companies providing this service, a few examples are below:

www.ubiome.com

www.ubiota.com

www.americangut.org

www.gdx.net

www.truehealthlabs.com

Pets May Help the Gut!

 A study published in 2017, which included 746 babies found that exposure to pets while in utero and after birth promotes gut microbes that lower the risk of allergies and obesity.



- Ruminococcus and Oscillospira microbes were elevated in infants regardless of method of delivery.
- The bacteria, Enterobacteria was also decreased in infants who were exposed to pets. This type of bacteria is associated with food poisoning such as Salmonella. [35]

Bacteria in your gut and cancer therapy.

The type of bacteria you have in your gut, will determine body response to cancer treatment with immunotherapy, which boosts the bodies own defenses to fight tumors.

One study, at the Gustave Roussy Cancer Campus in Paris, examined 249 patients with lung or kidney cancer receiving immunotherapy in form of drug class called immune checkpoint inhibitors (ICI). Those patients, who had taken antibiotics, such as for dental infection, damaged their microbiome and were more likely to see tumours grow while on immunotherapy.

One species of bacteria in particular, Akkermansia muciniphila, was in 69 percent of patients that did respond compared with just a third of those who did not. Fecal microbiota transplantation (FMT) from cancer patients who responded to ICI (but not from non-responding patients) into germ-free or antibiotic treated mice ameliorated the antitumor effects of therapy. [36]

In another study at the University of Texas MD Anderson Cancer Center, 112 patients with advanced melanoma, reated with immumotherapy had their microbiome analysed.

Those that responded to therapy tended to have a richer, more diverse microbiome than those that did not. High levels of Faecalibacterium and Clostridiales appeared to be beneficial, while Bacteroidales species were associated with poor response to therapy. Germ-free mice (with melanoma) receiving fecal transplants from responding patients experienced enhanced antitumor effects of treatment. [37]

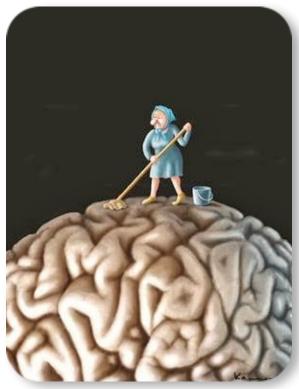
References:

- 1. Abbott, A., Scientists bust myth that our bodies have more bacteria than human cells. Nature News, 2017.
- 2. Fu, J., et al., The Gut Microbiome Contributes to a Substantial Proportion of the Variation in Blood Lipids. Circ Res, 2015. 117(9): p. 817-24.
- 3. Ridaura, V.K., et al., Cultured gut microbiota from twins discordant for obesity modulate adiposity and metabolic phenotypes in mice. Science, 2013. 341(6150).
- 4. Yano, J.M., et al., Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell, 2015. 161(2): p. 264-76.
- 5. Sudo, N., et al., Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice. J Physiol, 2004. 558(Pt 1): p. 263-75.
- 6. Savignac, H.M., et al., Bifidobacteria exert strain-specific effects on stress-related behavior and physiology in BALB/c mice. Neurogastroenterol Motil, 2014. 26(11): p. 1615-27.
- 7. Desbonnet, L., et al., Effects of the probiotic Bifidobacterium infantis in the maternal separation model of depression. Neuroscience, 2010. 170(4): p. 1179-88.
- 8. Messaoudi, M., et al., Assessment of psychotropic-like properties of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in rats and human subjects. Br J Nutr, 2011. 105(5): p. 755-64.
- 9. Steenbergen, L., et al., A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. Brain Behav Immun, 2015. 48: p. 258-64.
- 10. Alcock, J., et al., Is eating behavior manipulated by the gastrointestinal microbiota? Evolutionary pressures and potential mechanisms. BioEssays, 2017. 36(10): p. 940-949.
- 11. Rezzi, S., et al., Human metabolic phenotypes link directly to specific dietary preferences in healthy individuals. J Proteome Res, 2007. 6(11): p. 4469-77.
- 12. Thompson, R.S., et al., Dietary Prebiotics and Bioactive Milk Fractions Improve NREM Sleep, Enhance REM Sleep Rebound and Attenuate the Stress-Induced Decrease in Diurnal Temperature and Gut Microbial Alpha Diversity. Front Behav Neurosci, 2016. 10: p. 240.
- 13. Sampson, T.R., et al., Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease. Cell, 2016. 167(6): p. 1469-1480.e12.
- 14. News, A. Why Do Onions Make You Cry? Netscape What's New. 2017; Available from: http://isp.netscape.com/whatsnew/package.jsp?name=fte/onions/onions.
- 15. Eyerly, J., The gut makeover: 4 weeks to get healthy, lose weight and boost your brain. 2015: London Quercus Editions.
- 16. J, L.K.a.H., Microbiome restoration diet improves digestion, cognition and physical and emotional wellbeing. PubMed NCBI. PLoS One, 2017. 12(6).
- 17. Jones, S.E. and J. Versalovic, Probiotic Lactobacillus reuteri biofilms produce antimicrobial and anti-inflammatory factors. BMC Microbiol, 2009. 9: p. 35.
- 18. Yan, F., et al., Soluble proteins produced by probiotic bacteria regulate intestinal epithelial cell survival and growth. Gastroenterology, 2007. 132(2): p. 562-75.
- 19. Ng, S.C., et al., Immunosuppressive effects via human intestinal dendritic cells of probiotic bacteria and steroids in the treatment of acute ulcerative colitis. Inflamm Bowel Dis, 2010. 16(8): p. 1286-98.

- 20. Rousseaux, C., et al., Lactobacillus acidophilus modulates intestinal pain and induces opioid and cannabinoid receptors. Nat Med, 2007. 13(1): p. 35-7.
- 21. David, L.A., et al., Diet rapidly and reproducibly alters the human gut microbiome. Nature, 2013. 505: p. 559-563.
- 22. Society, A.C. The precise reason for the health benefits of dark chocolate: mystery solved American Chemical Society. 2014; Available from: https://www.acs.org/content/acs/en/pressroom/newsreleases/2014/march/the-precise-reason-for-the-health-benefits-of-dark-chocolate-mystery-solved.html.
- 23. Perez-Cornago, A., et al., Intake of High-Fat Yogurt, but Not of Low-Fat Yogurt or Prebiotics, Is Related to Lower Risk of Depression in Women of the SUN Cohort Study. J Nutr, 2016. 146(9): p. 1731-9.
- 24. Lee, A., et al., Consumption of Dairy Yogurt Containing Lactobacillus paracasei ssp. paracasei, Bifidobacterium animalis ssp. lactis and Heat-Treated Lactobacillus plantarum Improves Immune Function Including Natural Killer Cell Activity. Nutrients, 2017. 9(6).
- 25. Cervantes-Barragan, L., et al., Lactobacillus reuteri induces gut intraepithelial CD4+CD8alphaalpha+ T cells. Science, 2017. 357(6353): p. 806-810.
- 26. Byerley, L.O., et al., Changes in the gut microbial communities following addition of walnuts to the diet. J Nutr Biochem, 2017. 48: p. 94-102.
- 27. Menni, C., et al., Omega-3 fatty acids correlate with gut microbiome diversity and production of N-carbamylglutamate in middle aged and elderly women. Sci Rep, 2017. 7(1): p. 11079.
- 28. Hjorth, M.F., et al., Pre-treatment microbial Prevotella-to-Bacteroides ratio, determines body fat loss success during a 6-month randomized controlled diet intervention. Int J Obes (Lond), 2017.
- 29. Smits, S.A., et al., Seasonal cycling in the gut microbiome of the Hadza hunter-gatherers of Tanzania. Science, 2017. 357(6353): p. 802-806.
- 30. Adnan, S., et al., Alterations in the gut microbiota can elicit hypertension in rats. Physiological Geonomics, 2016.
- 31. Chassaing, B., et al., Colonic Microbiota Encroachment Correlates With Dysglycemia in Humans. Cell Mol Gastroenterol Hepatol, 2017. 4(2): p. 205-221.
- 32. Hirsch, B.E., et al., Effectiveness of fecal-derived microbiota transfer using orally administered capsules for recurrent Clostridium difficile infection, in BMC Infect Dis, B. Central, Editor. 2015.
- 33. Vassallo, G., et al., Review article: Alcohol and gut microbiota the possible role of gut microbiota modulation in the treatment of alcoholic liver disease. Aliment Pharmacol Ther, 2015. 41(10): p. 917-27.
- 34. Clarke, S.F., et al., Exercise and associated dietary extremes impact on gut microbial diversity. Gut, 2014. 63(12): p. 1913-20.
- 35. Tun, H.M., et al., Exposure to household furry pets influences the gut microbiota of infant at 3-4 months following various birth scenarios. Microbiome, 2017. 5(1): p. 40.
- 36. Routy, B., et al., Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors. Science, 2017.

37.	Gopalakrishnan, Yimmunotherapy in n		response	to	anti-PD-1

Purpose of sleep: formation and deletion of memories as well as the ultimate "brain washer"



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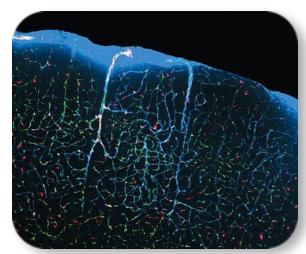
A mouse study suggests that sleep helps restore the brain by flushing out toxins that build up during waking hours. The results point to a potential new role for sleep in health and disease.

Scientists recently discovered a system that drains waste products from the brain. Cerebrospinal fluid, (clear liquid surrounding the brain and spinal cord) moves through the brain along a series of channels that surround blood vessels. The system is regulated by the brain's glial cells, and is called glymphatic system. Glymphatic system helps removing a toxic protein known as beta-amyloid from brain tissue.

(Beta-amyloid accumulates in the brains of patients with Alzheimer's disease causing disruption in brain function). Brain levels of beta-amyloid decrease during sleep. The researcher's first injected dye into the cerebrospinal fluid of mice and monitored brain activity as they tracked the dye flow through the animals' brains. There was minimal flow of dye when the mice were awake but brisk flow was seen during sleep. Changes in the way fluid moves through the brain between

conscious and unconscious states may reflect differences in the space available for movement. Scientist discovered that extracellular volume (space outside brain cells) increased by 60 percent in the brain's cortex when the mice were asleep.

Cerebrospinal fluid (blue) flows through the brain and clears out toxins through a series of channels that expand during sleep.



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Sleep

After injecting mice with labeled (easy to trace) beta-amyloid and measuring how long it lasted in their brains when they were asleep and awake, beta-amyloid disappeared twice as quickly in the brains of mice that were asleep!

Glial cells control flow through the glymphatic system by shrinking and swelling. The hormone noradrenaline (a stress hormone), which increases alertness, is known to cause cells to swell. Treating mice with drugs that block noradrenaline induced a sleep-like state and increased brain fluid flow and extracellular brain volume. This result suggests a molecular connection between the sleep-wake cycle and the brain's cleaning system and may lead to future treatments of Alzheimer's disease. [1]

Stages of sleep

Every 60-100 minutes we go through a cycle of four stages of sleep:

- Stage 1 is a drowsy, relaxed state between being awake and sleeping breathing slows, muscles relax, heart rate drops.
- Stage 2 is slightly deeper sleep you may feel awake and this means that, on many nights, you may be asleep and not know it.
- Stage 3 and Stage 4, or Deep Sleep it is very hard to wake up from Deep Sleep because this is when there is the lowest amount of activity in your body.
- After Deep Sleep, we go back to Stage 2 for a few minutes, and then enter Dream Sleep also called REM (rapid eye movement) sleep, which as its name suggests, is when you dream.

In a full sleep cycle, a person goes through all the stages of sleep from one to four, then back down through stages three and two, before entering dream sleep.

The Myth of 8 hours sleep...[2]

- We frequently worry about lying awake in the middle of the night but this may be something completely natural. A growing body of evidence from both science and history suggests that the eight-hour sleep may be not be what nature intended.
- A study observed a group of healthy volunteers exposed to 14 hour of darkness a day for 30 days. By fourth week a very distant sleep pattern emerged. They slept first for four hours, and then woke for one or two hours before falling into a second four-hour sleep.[3]
- The study was very well received, among the general public the idea that we must sleep for eight consecutive hours persists.

Sleep

History of sleep

In 2001, historian Roger Ekirch of Virginia Tech published a seminal paper, drawn from 16 years of research (with over 500 references), revealing a wealth of historical evidence that humans used to sleep in two distinct parts since ancient times. Those references describe a first sleep which began about two hours after dusk, followed by waking period of one or two hours and then a second sleep. During this waking period people were quite active. They often got up, went to the toilet or smoked tobacco and some even visited neighbors. Most people stayed in bed, read, wrote and often prayed. Countless prayer manuals from the late 15th Century offered special prayers for the hours in between sleeps. People often chatted to bed-fellows or had sex. The first and second sleep started to disappear during the late 17th Century. It started among the urban upper classes in northern Europe and over the course of the next 200 years filtered down to the rest of Western society. This shift was improvements in street and domestic lighting and a surge in coffee houses - which were sometimes open all night. As the night became a place for legitimate activity (rather than place of robbery and prostitution) and as that activity increased, the length of time people could dedicate to rest was reduced significantly. By the 1920s the idea of a first and second sleep had receded entirely from our social consciousness forced largely by shift work. [3]

Most of us when we wake up middle of the night, we panic thinking about the workday ahead and of course unable to fall asleep again. Relax, this is how nature originally intended us to sleep. Read, pray, meditate!

Evolution of sleep

700 Million Years of Melatonin

Melatonin (the hormone of "darkness") is a hormone that is produced by the pineal gland in animals and regulates sleep and wakefulness. It is involved in the synchronization of the circadian rhythms including sleep-wake timing, blood pressure regulation, seasonal reproduction, and many others. Researchers discovered that melatonin was around for at least 700 million years based on a discovery of circadian cycle in a rather distantly related invertebrate a marine worm called Platynereis dumerilii.[4]

Down from the trees we finally got some good (REM) sleep...

Researchers conducted sleep pattern studies of 19 primate species and found wide variations in how long the animals slept. Mouse lemurs doze for seventeen hours a day, for example, while humans sleep just seven hours or so a day which was the least of any primate on the planet. Humans spend about 22 percent of sleep in REM, the highest ratio of REM to total sleep in any primate. As you can imagine it was not easy for our monkey-like ancestors to reach REM sleep. They slept on branches, and their nights were anything but pleasant. As monkeys try to sleep, they get awaken



by winds, tree snakes and the jostling of their fellow primates. 20 million years ago, the ancestors of humans and other apes changed their sleeping habits because they became too big for branches. Today, no primate that weighs over 60 pounds sleeps on a branch. Instead, chimpanzees, bonobos and their cousins build sleeping platforms each night from sticks and other materials.

Apes aim to get the best night's rest they can. Early human ancestors continued to sleep in trees until about two million years ago. By 1.8 million years ago, new hominins like Homo erectus had left the trees. Early humans slept around fires in large groups, able to ward off predators. The result was the chance to get an even better night's rest. Humans were able to fall more soundly asleep and to experience deeper bouts of REM sleep.



Since it took less time to get the benefits of REM sleep, humans were able to get by with less sleep over all than other primates. They gained a few extra waking hours each day, which they might have used to make new tools or share stories.[5]

Living Another Day, Thanks to Grandparents Who Couldn't Sleep

Recent study of a Kenyan Hadza tribe of hunters and gatherers suggests that the way sleep patterns change with age may be an evolutionary adaptation that helped our ancestors survive the night by ensuring one person in a community was awake at all times. The researchers called this phenomenon the "poorly sleeping grandparent hypothesis," suggesting that an older member of a



community who woke before dawn might have been crucial to spotting the threat of a hungry predator while younger people were still asleep. It may explain why people slept in mixed-age groups through much of human history. Out of more than 220 total hours of sleep observation, researchers found only 18 minutes when all adults were sound asleep simultaneously. Typically, older participants in their 50s and 60s went to bed earlier and woke up earlier than those in their 20s and 30s. On average, more than a third of the group was alert, or lightly dozing, at any given time.[6]

Whatever gets you out of bed can help you sleep

Older adults who have a purpose in life are more likely to have fewer sleep disturbances such as sleep apnea and restless leg syndrome and sleep better over a long period of time. Study included 823 participants individuals without dementia, 60 to 100 years old with an average age of 79. More than half were African American and 77 percent were female. People who felt their lives had meaning were 63 percent less likely to have sleep apnea and 52 percent less likely to have restless leg syndrome. They also had moderately better sleep quality, a global measure of sleep disturbance. Participants answered a 10-question survey on purpose in life and a 32-question survey on sleep. For the purpose in life survey, they were asked to rate their response to such statements as, "I feel good when I think of what I've done in the past and what I hope to do in the future." [7]

• Both excessively long and short-term sleep durations are risk factors of cardiovascular outcomes. [8]

Short-term Sleep (less than 7 hours)

- Low-grade inflammation (in the cardiovascular system) is activated during short sleep.
- The greatest risk increase was associated with those who slept fewer than five hours a night.[9] One extra hour of sleep per night is associated with a 33 percent reduction in the development



- of calcium deposits in coronary arteries, which can lead to heart disease.[10]
- Short duration sleep is linked to increased appetite, reduced energy expenditure and low-grade inflammation.

Sleeping less than 6 hours per night kills!

- 1,741 of individuals underwent sleep study and were followed for 16 years.
- CVD (cardiovascular disease) was defined by a history of heart disease, including hypertension or diabetes, and CBV (cerebrovascular disease) by a history of stroke.
- Polysomnographic (sleep study) total sleep time was classified as normal (6 hours or more) or short (less than 6 hours) duration.
- Risk of mortality associated with CVD and stroke was enhanced in those who slept less than 6 hours in the lab; specifically, their risk of mortality was 1.8-fold and 2.4-fold, respectively.
- In contrast, in individuals who slept more than 6 hours in the lab, the risk of mortality associated with CVD or stroke was not significantly increased. Presented at Julio Fernandez-Mendoza, PhD SLEEP 2017: 31st Annual Meeting of the Associated Professional Sleep Societies.
- A study "Sleep Matters" suggested that there is a link between insomnia and poor relationships, low energy levels and lack of concentration (in addition to prior links to depression, immune deficiency and heart disease).

Insomniacs are:

- Four times as likely to have relationship problems.
- Three times as likely to feel depressed.
- Three times as likely to suffer from lack of concentration.[11]
- A 2017 study including 16,000 patients found that those who had problems initiating sleep, maintaining sleep, and those with non-restorative sleep had 27 percent, 11 percent, and 18 percent increases in the risk of stroke and cardiovascular events. [12]

Long-term Sleep

- An association was also found between regular sleep over nine hours and early death.
- Stick to the ideal six to eight hours per night when possible.[13]

Obstructive Sleep Apnea (OSA)

• Symptoms including frequent awakenings during the night, excessive snoring and daytime drowsiness, exposes the cardiovascular system to oxidative stress. Therefore, people with OSA have a higher risk of developing aggressive atherosclerosis (blockages or narrowing in the arteries). [14]



• Sleep apnea is linked with increased risk of atrial fibrillation, stroke, hypertension, dementia, depression, low heart rate (sometimes requiring implantation of a pacemaker) erectile dysfunction, heart failure and other conditions.

Properly Treating OSA May Be Beneficial For Heart, Blood Sugar: Research suggests that properly treating obstructive sleep apnea benefits not only the heart but also glucose metabolism. Investigators found that if individuals with OSA don't use machines at night to help keep the airway open, measures of their heart health and blood sugar worsen: glucose, free fatty acids, heart rate and blood pressure were all elevated.[15]

Snoring (with and without apnea)

- Vibrations from snoring damage the layer of cells that line the inner part of blood vessels, triggering inflammation. [16]
- Adults who reported frequent loud snoring had twice the risk of developing metabolic syndrome conditions, such as obesity, high blood pressure and diabetes, in a three-year follow-up.



• Snoring can cause memory and cognitive problems about 12 years earlier than in those who don't snore according to a 2014 study. [17]

Duration and quality are both important!

- Short: Less than 6 hours had a 15 percent higher risk of cardiovascular disease and a 23 percent higher risk of coronary heart disease.
- Short sleepers with poor quality sleep had a 65 percent increased risk of cardiovascular disease and an 85 percent increased risk of coronary heart disease than patients with normal sleep duration with good sleep quality. [18]



Insomnia: a very costly problem! Treating insomnia costs the nation at least \$10 billion a year, and up to \$100 billion after adding cost of treatment medical problems (caused by insomnia), lost work time and productivity.

- To improve sleep quality here are six tips and have someone read to you, take a bath, make your bedroom dark, cool and quiet, use a weighed blanket, say your prayers and turn off your devices.
- For further information if you have problem falling asleep there is a several week on line course on how to overcome insomnia: cbtforinsomnia.com. Cognitive behavioral therapy is superior to sleeping pills without any side effects! It is currently the recommended approach rather than sleeping pills.[19]

The dark side of sleeping pills

- The number of emergency room visits involving overmedication of zolpidem the active ingredient in some prescription sleeping pills (Ambien) almost doubled between 2005 and 2010, increasing from 21,824 visits in a two-year period to 42,274.
- Almost 70 percent of patients were females (as women metabolize sleeping pills slower).
- Side effects linked to sleeping pills include hallucinations, sleepwalking, sleep driving, sleep eating, amnesia, and depression.
- Sleeping pills generally only increase the amount of time you sleep by a matter of minutes, and far from waking up refreshed, they can impair your functioning the next day, making you even less alert and more disoriented than after sleepless night!
- Belsomra in clinical trials, the drug allowed people to fall asleep six minutes sooner than those taking a placebo, and stay asleep 16 minutes longer.

- Ambien, Lunesta, and Sonata reduced the average time it takes to fall asleep by about 13 minutes compared to placebo, while increasing total sleep time by about 11 minutes.
- Sleeping pills do not correct underlying cause of insomnia but cognitive behavioral therapy does!
- Receiving hypnotic prescriptions (sleeping pills) was associated with almost fourfold increase risk of death.
- Even when prescribed <18 pills/year there was still over 3x increase risk in death.



- This association held in separate analyses for several commonly used hypnotics and for newer shorter-acting drugs. Control of selective prescription of hypnotics for patients in poor health did not explain the observed excess mortality.
- Sleep medications linked to death in this study were benzodiazepines (for example temazepam), non-benzodiazepines (for example Ambien, Lunesta, and Sonata), barbiturates, and sedative antihistamines (such as Benadryl).
- In addition those who averaged over 132 sleeping pills per year were 35 percent more likely to develop a new cancer. [20]

Sleeping pills and dementia - see Chapter 8

References:

- 1. Xie, L., et al., Sleep Drives Metabolite Clearance from the Adult Brain. Science, 2013. **342**(6156).
- 2. Hegarty, S., *The myth of the eight-hour sleep BBC News*. BBC News Magazine, 2017.
- 3. Wehr, T.A., *In short photoperiods, human sleep is biphasic*. J Sleep Res, 1992. **1**(2): p. 103-107.
- 4. Tosches, M., et al., *Melatonin Signaling Controls Circadian Swimming Behavior in Marine Zooplankton*, in *Cell*. 2014, Elsevier. p. 46-57.
- 5. Samson, D.R., et al., *Sleep intensity and the evolution of human cognition*. Evolutionary Anthropology: Issues, News, and Reviews, 2017. **24**(6): p. 225-237.
- 6. Samson, D.R., et al., *Chronotype variation drives night-time sentinel-like behaviour in hunter–gatherers*. Proceedings of the Royal Society Biological Sciences, 2017.
- 7. Turner, A.D., C.E. Smith, and J.C. Ong, *Is purpose in life associated with less sleep disturbance in older adults?* Sleep Science and Practice, 2017. **1**(1): p. 14.
- 8. Cappuccio, F.P., et al., *Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies.* Eur Heart J, 2011. **32**(12): p. 1484-92.
- 9. Sabanayagam, C. and A. Shankar, *Sleep duration and cardiovascular disease: results from the National Health Interview Survey.* Sleep, 2010. **33**(8): p. 1037-42.
- 10. King, C.R., et al., *Short sleep duration and incident coronary artery calcification*. Jama, 2008. **300**(24): p. 2859-66.
- 11. @BBCWorld, *Insomnia damages relationships, according to study BBC News.* Health, 2011.
- 12. He, Q., et al., *The association between insomnia symptoms and risk of cardio-cerebral vascular events: A meta-analysis of prospective cohort studies.* Eur J Prev Cardiol, 2017. **24**(10): p. 1071-1082.
- 13. Cappuccio, F.P., et al., *Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies.* Sleep, 2010. **33**(5): p. 585-92.
- 14. Abro, J., et al., Abstract 210: Coronary Atherosclerosis and Coronary Artery Disease in Patients With Obstructive Sleep Apnea: Assessment at Coronary CT Angiography. Circulation, 2009. **120**(S302).
- 15. Chopra, S., et al., Obstructive Sleep Apnea Dynamically Increases Nocturnal Plasma Free Fatty Acids, Glucose, and Cortisol During Sleep. The Journal of Clinical Endocrinology & Metabolism, 2017. **102**(9): p. 3172-3181.
- 16. Troxel, W.M., et al., Sleep symptoms predict the development of the metabolic syndrome. Sleep, 2010. **33**(12): p. 1633-40.
- 17. Osorio, R.S., et al., *Sleep-disordered breathing advances cognitive decline in the elderly.* Neurology, 2015. **84**(19): p. 1964-71.
- 18. Hoevenaar-Blom, M.P., et al., *Sleep duration and sleep quality in relation to 12-year cardiovascular disease incidence: the MORGEN study.* Sleep, 2011. **34**(11): p. 1487-92.
- 19. Trockel, M., et al., Cognitive Behavioral Therapy for insomnia with Veterans: evaluation of effectiveness and correlates of treatment outcomes. Behav Res Ther, 2014. **53**: p. 41-6.

20. Kripke, D.F., R.D. Langer, and L.E. Kline, *Hypnotics' association with mortality or cancer: a matched cohort study.* BMJ Open, 2012. **2**(1): p. e000850.



Preserving and Expanding Your Memory

Dementia

Starting at age 65, the risk of developing the disease doubles every 5 years. By age 85 years and older, between 25 percent and 50 percent of people will exhibit signs of Alzheimer's disease. Up to 5.3 million Americans currently have Alzheimer's disease. By 2050, the number is expected to more than double due to the aging of the population. Alzheimer's disease is the sixth leading cause of death in the United States and is the fifth leading cause among persons age 65 and older. In spite of more than 100 ongoing clinical trials, no drug has been shown to cure or halt dementia. More than 200 experimental drugs intended to treat if failed in the past 30 years. But there is hope!

The following types of memory lapses are normal among older adults and generally are *not* considered warning signs of dementia:

- Occasionally forgetting where you left things you use regularly, such as glasses or keys.
- Forgetting names of acquaintances or blocking one memory with a similar one, such as calling a grandson by your son's name.
- Occasionally forgetting an appointment or walking into a room and forgetting why you entered.
- Becoming easily distracted or having trouble remembering what you've just read, or the details
 of a conversation.
- Not quite being able to retrieve information you have "on the tip of your tongue."

Common Risk Factors for Dementia

- Age: The risk goes up with advanced age. This is the strongest risk factor of all.
- Alcohol use: Most studies suggest that drinking large amounts of alcohol increases the risk of dementia, while drinking a moderate amount may be protective.
- Atherosclerosis: The accumulation of fats and cholesterol in the lining of arteries, coupled with an inflammatory process that leads to a thickening of the vessel walls (known as atherosclerosis), can hinder blood from getting to the brain, which can lead to stroke or another brain injury. For example, high levels of low-density lipoprotein (LDL, or "bad" cholesterol) can raise the risk for vascular dementia. High LDL levels also have been linked to AD.
- Diabetes: People with diabetes appear to have a higher risk for dementia, although the evidence for this association is modest. Poorly controlled diabetes, however, is a well-proven risk factor for stroke and cardiovascular disease-related events, which in turn increase the risk for vascular dementia.

Explanation of the link between diabetes and Alzheimer's disease.

Excess glucose leads to damages of a vital enzyme involved with inflammation response to the early stages of Alzheimer's. In Alzheimer's disease, abnormal proteins aggregate to form plaques and tangles in the brain which progressively damage the brain and lead to severe cognitive decline. Excessive glucose and its break-down products can damage proteins in cells via a reaction called glycation. By studying brain samples from people with and without Alzheimer's using a sensitive technique to detect glycation, researchers discovered that in the early stages of Alzheimer's glycation damages an enzyme called MIF (macrophage migration inhibitory factor) This particular enzyme is involved in the response of brain cells called glia to the build-up of abnormal proteins in the brain during Alzheimer's disease. Inhibition and reduction of MIF activity caused by glycation seems to be the 'tipping point' in disease progression: as Alzheimer's progresses, glycation of these enzymes increases. [1]

- *Genetics*: One's likelihood of developing a genetically linked form of dementia increases when more than one family member has the disorder.
- *Hypertension*: High blood pressure has been linked to cognitive decline, stroke, and types of dementia that affect the white matter regions of the brain.

Fluctuating blood pressure as a risk factor Alzheimer disease.

In a study of 1,674 (During the follow-up, 194 subjects developed all-cause dementia) Japanese individuals who were 60 or older and measured their blood pressure each morning for a month, those with the most variable readings had more than twice the risk of being diagnosed with

vascular dementia or Alzheimer's disease within 5 years vs those with stable readings. The findings suggest that adequately treating hypertension and maintaining a healthy lifestyle with low mental or physical stress and good sleep habits "could contribute to lower the blood-pressure variability, which might then lead to reduced risk of dementia. [2]

- *Mental illness:* Depression has been associated with mild mental impairment and cognitive function decline.
- *Smoking*: Smokers are prone to diseases that slow or stop blood from getting to the brain.
- *Midlife stress*: strong predictor of dementia later in life: see chapter 4.
- *Head injury:* There may be a strong link between serious head injury and future risk of Alzheimer's, especially when trauma occurs repeatedly or involves loss of consciousness.
- *Sleep apnea*: The presence of sleep apnea was associated with an earlier age at cognitive decline. CPAP treatment of sleep apnea may delay progression of cognitive impairment![3]

Nine factors that most significantly contribute to the risk of dementia: 2017 Lancet Commission on dementia prevention, intervention and care.

Factors	Risk %
Mid-life hearing loss	9%
Failing to complete secondary education	8%
Smoking	5%
Failing to seek early treatment for depression	4%
Physical inactivity	3%
Social isolation	2%
High blood pressure	2%
Obesity	1%

These risk factors - which are described as potentially modifiable - add up to 35 percent. The other 65 percent of dementia risk is thought to be potentially non-modifiable. The report, which combines the work of 24 international experts, indicates that lifestyle factors play a major role in increasing or reducing an individual's dementia risk.

It examines the benefits of building a "cognitive reserve", which means strengthening the brain's networks so it can continue to function in later life

despite damage. Failure to complete secondary education was a major risk factor, and the authors suggest that individuals who continue to learn throughout life are likely to build additional brain reserves.

Key message from the report is that what is good for the heart is good for the brain. Not smoking, doing exercise, keeping a healthy weight, treating high blood pressure and diabetes can all reduce the risk of dementia, as well as cardiovascular disease, and cancer.[4]

Vision loss leads to memory loss as well

Brain to function properly need constant stimulation delivered via vison and hearing.

In a cross-sectional study of 2 nationally representative samples of the US population over 33 000 participants), visual impairment measured at distance, near, and by self-report was associated with 1.9- to 2.8-fold higher odds of cognitive dysfunction or dementia after adjustment for other known dementia risk factors. [5]

To prevent dementia, start early!

The Life's Simple 7 guidelines promote heart health by urging people to maintain a healthy blood pressure, control cholesterol levels, reduce blood sugar, engage in regular physical activity, eat better, lose weight, and either quit or avoid smoking. 518 people participating in a long-range heart health study.

The participants, now an average age of 51, had been followed for three decades. They have received follow-up exams every two to five years, and had brain scans 25 years after entering the study, the researchers said in background information.

The research team rated each participant based on how well they followed each of Life's Simple 7 at the start of the study. A person received scores between zero and 2 points for each recommendation, depending on how closely they followed it, with a maximum heart healthy score of 14

Researchers then compared those scores against the brain scans performed in middle age, to see whether living healthy as a young adult mattered years later.

Each 1-point improvement in a young person's heart-healthy lifestyle score was essentially the same as one year less in brain aging. As the score increases, you see a better result for brain structure.

However, not all the heart association's recommendations carried the same weight. Smoking had a stronger association with smaller brain volume than the other lifestyle factors, the researchers found.[4]

Medications strongly linked to dementia

• Anticholinergic drugs are linked with cognitive impairment and an increased risk of dementia.

- Examples of these medications include: Benadryl, Demerol, Dimetapp, Dramamine, Paxil, Unisom and VESIcare.
- They are sold over the counter and by prescription as sleep aids and for chronic diseases including hypertension, cardiovascular disease and chronic obstructive pulmonary disease.
- Cognitive tests revealed that people taking anticholinergic drugs performed worse on shortterm memory tests, as well as on some tests of executive function, including verbal reasoning, planning and problem solving.
- Anticholinergic drug users also showed lower levels of glucose metabolism a biomarker for brain activity both in the brain overall and in the hippocampus, a region of the brain associated with memory and which has been identified as affected early by Alzheimer's disease. The participants using anticholinergic drugs were also found to have reduced brain volume and larger ventricles, the cavities inside the brain.
- Drugs with a strong anticholinergic effect cause cognitive problems when taken continuously for as few as 60 days. Drugs with a weaker effect could cause impairment within 90 days.[6]
- For a complete list of anticholinergic drugs linked to memory loss go to:

 (http://www.agingbraincare.org/uploads/products/ACB_scale_-legal_size.pdf)

Sleeping pills and other sedatives

- Benzodiazepines (this includes most commonly prescribed sleeping pill: Ambien) are a class of drugs used to treat short-term insomnia, anxiety, and sometimes epilepsy.
- Although clinical guidelines recommend against the long-term use of benzodiazepines, particularly in elderly people with a greater risk of side effects, chronic benzodiazepine use is common in older populations.



- A 2014 study reported that people who had used benzodiazepines for more than three months had almost a 50 percent higher risk of Alzheimer's disease over the following six years, an association that has been reported previously.
- Short-term use of benzodiazepines (less than 91 daily doses) did not raise the risk for Alzheimer's but, beyond that point, with longer use came greater risk.
- The associated risk was observed even in people who had previously used a benzodiazepine for at least six months but had stopped using it at least a year before their diagnosis of dementia. [7]

Weight and dementia

- There are conflicting reports on this issue. Initially smaller studies suggested that being overweight and obese increases risk of dementia both of Alzheimer and vascular type. But in a biggest study to date (Published in a highly respected Journal Lancet) of 2 million individuals with follow-up period of 9 years, 45,507 adults were diagnosed with dementia.
- The researchers found that, compared with adults who had a healthy BMI (between 20-25 kg/m²), those who were underweight defined in this study as a BMI less than 20 kg/m² during middle age were 34 percent more likely to be diagnosed with dementia.
- This increased risk remained for 15 years after adults' underweight status was recorded. The researchers also found that middle-aged adults' risk of dementia steadily reduced as their BMI increased. Compared with adults who had a healthy BMI, those who were severely obese (BMI greater than 40 kg/m²) were 29 percent less likely to develop dementia. [8]

Hearing and Memory

- A 2013 study including 2,000 participants, average age 77, found that those with hearing loss that was enough to interfere with conversation had a 24 percent higher chance of diminished cognitive abilities. [9]
- Another 2011 study consisting of 639 people followed for 12 to 18 years found that those who had moderate hearing loss has triple the risk of dementia. [10]



• Hearing aids can improve cognitive scores according to a 2015 study. In a group of 94 people age 65 to 85, after one year of hearing aid implantation more than 80 percent of the participants with low cognitive scores saw an increase in scores. [11]

Memory and Sleep

- Sleep position can actually affect and protect you against Alzheimer's.
- A 2015 study found that sleeping in the lateral position (side) is the best for your brains process of cleaning out toxins such as beta amyloid and tau proteins which are associated with Alzheimer's disease. [12]



- Another 2014 study including 2,822 men found that those who had difficulties sleeping had an increased risk of developing Alzheimer's by 1.5 times compared to those who do not have sleeping problems. [13]
- Not only does sleep position matter, but amount of sleep affects cognition too! A 2009 study looked at sleep deprived mice and found that the less sleep the mice got, the more quickly amyloid plaques developed in the brain which is associated with Alzheimer's. [14]
- Just as too little sleep can increase risk for Alzheimer's, too much sleep may also!
- A 2016 study of 2,457 adults found that sleeping more than nine hours increases the risk of all-cause dementia 2.4 times and Alzheimer's 2.2 times.
- The study also linked longer sleep periods with poorer cognitive function and smaller cerebral brain volume. [15]

Survived heart attack. What's next? Dementia...

Danish researchers studied 314,911 heart attack patients and compared them with 1,573,193 controls that had not had a heart attack. During 35 years of follow-up, there were 3,615 cases of Alzheimer's disease, 2,034 cases of vascular dementia and 5,627 cases of other dementias among the heart attack patients.

There was no association of heart attack with Alzheimer's disease. But heart attack increased the risk for vascular dementia, the type caused by impaired blood flow to the brain, by 35 percent. This is not surprising as both conditions share the same etiology: high blood pressure, tobacco abuse and others. [16]

Want to decrease your brain power? Put a smart phone next to you!

The mere presence of one's smartphone (even when is off!) reduces available cognitive capacity and impairs cognitive functioning, even though people feel they're giving their full attention and focus to the task at hand. The explanation is that trying to focus on a task next to a smart phone requires effort not to be distracted by it: brain drain! [17]



Diet & Memory

Eating Mediterranean Foods May Equal Five Fewer Years of Brain Shrinkage!!!!!

Among older adults, Mediterranean diet adherence was associated with less brain atrophy, with an effect similar to 5 years of aging. Higher fish, olive oil and lower red meat intake might be the key food elements that contribute to the benefits of Mediterranean diet on brain structure.[18]

Healthy brain aging and omega-3 PUFAs

Recent data demonstrated that fluid intelligence may be optimally supported by specific omega-3 PUFAs through preservation of gray matter of a specific part of brain (called frontoparietal cortex) structure in cognitively intact older adults. Those specific omega 3 PUFAs were alpha-linolenic acid (found in kale, spinach, purslane, soybeans, walnutsand many seeds such as chia, flax and hemp seeds.) Stearidonic acid, (sources: seed oils, such as hemp and certain fish, such as sardines and herring); and algae and eicosatrienoic acid. [19]



Alzheimer disease and omega-3 PUFAs

Researchers discovered that omega-3 fatty acids, which are found in fish oil, could facilitates the clearance of waste from the brain, including amyloid-β peptides, which is crucially involved in Alzheimer's disease. Scientists first used mice to investigate the effect of omega-3 PUFAs on the clearance of waste from the brain. Compared to the wild-type mice, the experimental mice with enriched endogenous omega-3 PUFAs (mice engineered to make omega 3) significantly promote the clearance function in the brain, including the Aβ clearance from the brain. When wild-type mice were supplemented with fish oil, which contains high concentrations of omega-3 PUFAs, researchers found that fish oil-supplemented mice also improved the clearance function in the brain. The effect is mediated by activating so called glymphatic system (see chapter 7), which is essentially a sewer system of our brain (which you do not want to clog!) [20]

Author's comment:

If your house mouse looks confused, forgetful, give him a small serving of fish (preferably salmon) and walnuts, both excellent sources of omega 3!





Confused House Mouse

Non-Confused House Mouse

• There is new evidence that changing your gut bacteria improves cognitive function, see: Human Microbiome / Chapter 6.

Chocolate consumption affects cognitive ability

• Consuming chocolate is significantly associated with superior visual-spatial memory and organization, working memory, scanning and tracking, abstract reasoning, and the mini-mental state examination. These functions translate to everyday tasks, such as remembering a phone number, or your shopping list, or being able to do two things at once, like talking and driving at the same time. [21]

Coffee

- Findings from the Italian Longitudinal Study on Aging suggested that cognitively normal older individuals who never or rarely consumed coffee and those who increased their coffee consumption habits had a higher risk of developing MCI. (Mild cognitive impairment).
- Therefore, moderate and regular coffee consumption may have neuroprotective effects also against MCI, confirming previous studies on the long-term protective effects of coffee, tea, or caffeine consumption and plasma levels of caffeine against cognitive decline and dementia. [22]

Cherry Juice

- A 2015 study found that drinking anthocyaninrich cherry juice can increase cognitive function!
- Anthocyanins are a subgroup of flavanols is found in high concentrations in fruits, vegetables, wine tea and cocoa.
- Just after 12 weeks of cherry juice consumption (200 ml/day) resulted in increased verbal fluency, short-term memory and long-term memory. Participants also saw a decrease in systolic and diastolic blood pressure. [23]



• Similar effect was seen in 12 weeks of daily wild blueberry juice supplementation (equivalent to almost a 1 lb. of blueberries). [24]

Exercise

Most powerful tool to prevent dementia (60% of dementia can be prevented with physical activity) and grow new brain cells mediated by release of a potent growth factor cathepsin B. (see chapter 3)



Yoga and Meditation

The best way to protect your memory? YOGA: Stretching and meditation are better at preventing dementia than brain training games!

- Scientists recruited 25 volunteers over the age of 55 who had reported memory issues such as forgetting names and faces, missing appointments or misplacing belongings. They split them into two groups, with one carrying out memory exercises and the other yoga and meditation. After three months both were equally good at improving verbal memory skills, which help people remember names and word lists however the spiritual path provided added benefits in the form of enhanced visual-spatial memory (which comes into play when recalling locations and navigating while walking or driving, and helps reduce anxiety. Eleven participants received weekly hourlong memory training sessions and performed exercises ranging from crossword puzzles to computer-based tasks. The other 14 were given an hourlong yoga session once a week and meditation at home for 20 minutes every day.
- After 12 weeks, the scientists saw similar verbal memory improvements in both groups of volunteers. However, visual-spatial memory was increased to a greater degree in the yogameditation group.
- Participants practicing yoga and meditation were also less likely to be depressed and anxious, and were better able to cope with stress.
- The memory improvements coincided with altered brain activity, which was monitored using functional magnetic resonance imaging (fMRI) brain scans. Changes in the way the brain cells connect with each other were seen in both groups, but they were only statistically significant in the people practicing yoga. [25]

Sex and Memory - See Chapter 9

What if you combine all of it??? Than you really prevent dementia!

FINGER: Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability. [26]

This study involved 631 men and women between ages 60 and 77. Control group received basic health advice and regular check of cardiovascular health.

Treatment group underwent following interventions:

- Diet: Mediterranean
- Exercise first 6 months strength training 102 week aerobic training 2-4x a week (30-45 min per session) and after 6 months strength training increase to 2-3x a week and aerobic training to 3-5 x a week (60 min per session).
- Computer program training to enhance executive function and mental speed, 2 years later the outcome was really stunning!
- Decline in Cognitive function 30 percent higher in control group.
- 83 percent improvement in executive function compared to control.
- 150 percent increase in processing speed.
- 40 percent performance increase in complex memory task (remembering long list for example)
- Even patient with a gene variant APOEe4 (predisposing them to Alzheimer disease) benefited from intervention.
- Intervention group who carried the risk gene had a slower rate of cellular aging measured by the length of telomeres (caps at the end of a chromosome).

Beet root juice (BRJ) +exercise = restoring brain connections!

This was a first experiment to test the combined effects of exercise and beetroot juice on functional brain networks in the motor cortex and secondary connections between the motor cortex and the insula, which support mobility

The above study included 26 men and women age 55 and older who did not exercise, had high blood pressure, and took no more than two medications for high blood pressure. Three times a week for six weeks, they drank a beetroot juice supplement called Beet-It Sport Shot one hour before a moderately intense, 50-minute walk on a treadmill. Half the participants received Beet-It containing 560 mg of nitrate; the others received a placebo Beet-It with very little nitrate.



Beets contain a high level of dietary nitrate, which is converted to nitrite and then nitric oxide (NO) when consumed. NO increases blood flow in the body, and multiple studies have shown it can increase exercise performance in people of various ages.

Nitric oxide goes to the areas of the body which are hypoxic, (needing oxygen,) and the brain is a heavy consumer of oxygen in our body. When we exercise, the brain's somatomotor cortex, which processes information from the muscles, sorts out the cues coming in from the body as such exercise strengthens the somatomotor cortex. Combining beetroot juice with exercise delivers even more oxygen to the brain and creates an excellent environment for strengthening the somatomotor cortex.

The exercise + BRJ group had brain networks that more closely resembled those of younger adults, showing the potential enhanced neuroplasticity (brains ability to adjust to new situation) conferred by combining exercise and BRJ consumption. [27]

- 1. Kassaar, O., et al., Macrophage Migration Inhibitory Factor is subjected to glucose modification and oxidation in Alzheimer's Disease. Sci Rep, 2017. 7: p. 42874.
- 2. Oishi, E., et al., *Day-to-Day Blood Pressure Variability and Risk of Dementia in a General Japanese Elderly Population: The Hisayama Study.* Circulation, 2017. **136**(6): p. 516-525.
- 3. Osorio, R.S., et al., *Sleep-disordered breathing advances cognitive decline in the elderly.* Neurology, 2015. **84**(19): p. 1964-71.
- 4. Gill Livingston, A.S., Vasiliki Orgeat, et al., *Dementia prevention, intervention, and care-The Lancet*. The Lancet, 2017.
- 5. Chen, S.P., J. Bhattacharya, and S. Pershing, *Association of Vision Loss With Cognition in Older Adults*. JAMA Ophthalmol, 2017. **135**(9): p. 963-970.
- 6. Risacher, S.L., et al., Association Between Anticholinergic Medication Use and Cognition, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults. JAMA Neurol, 2016. **73**(6): p. 721-32.
- 7. Gage, S.B.d., et al., *Benzodiazepine use and risk of Alzheimer's disease: case-control study.* BMJ, 2014(349).
- 8. Nawab Qizilbash, J.G., Michelle Johnson, et.al., *BMI and risk of dementia in two million people over two decades: a retrospective cohort study The Lancet Diabetes & Endocrinology.* The Lancet Diabetes & Endocrinology, 2017. **3**(6): p. 431-436.
- 9. Lin, F.R., et al., *Hearing Loss and Cognitive Decline in Older Adults*. JAMA Internal Medicine, 2013. **173**(4): p. 293-299.
- 10. Lin, F.R., et al., *Hearing Loss and Incident Dementia*. Archives of Neurology, 2011. **68**(2): p. 214-220.
- 11. Mosnier, I., et al., *Improvement of Cognitive Function After Cochlear Implantation in Elderly Patients*. JAMA Otolaryngology–Head & Neck Surgery, 2015. **141**(5): p. 442-450.
- 12. Lee, H., et al., *The Effect of Body Posture on Brain Glymphatic Transport*, in *J Neurosci*. 2015. p. 11034-44.
- 13. Blackwell, T., et al., Associations of objectively and subjectively measured sleep quality with subsequent cognitive decline in older community-dwelling men: the MrOS sleep study. Sleep, 2014. **37**(4): p. 655-63.
- 14. Kang, J.E., et al., *Amyloid-β Dynamics are Regulated by Orexin and the Sleep-Wake Cycle*. Science, 2009. **326**(5955): p. 1005-7.
- 15. Westwood, A.J., et al., *Prolonged sleep duration as a marker of early neurodegeneration predicting incident dementia.* Neurology, 2017. **88**(12): p. 1172-1179.
- 16. Sundboll, J., et al., *Higher Risk of Vascular Dementia in Myocardial Infarction Survivors*. Circulation, 2017.
- 17. Ward, A.F., et al., Brain Drain: The Mere Presence of One's Own Smartphone Reduces Available Cognitive Capacity. JACR, 2017. **2**(2).
- 18. Gu, Y., et al., *Mediterranean diet and brain structure in a multiethnic elderly cohort.* Neurology, 2015. **85**(20).

- 19. Zamroziewicz, M.K., et al., *Determinants of fluid intelligence in healthy aging: Omega-3 polyunsaturated fatty acid status and frontoparietal cortex structure.* Nutr Neurosci, 2017: p. 1-10.
- 20. Ren, H., et al., *Omega-3 polyunsaturated fatty acids promote amyloid-beta clearance from the brain through mediating the function of the glymphatic system.* Faseb j, 2017. **31**(1): p. 282-293.
- 21. Crichton, G.E., M.F. Elias, and A. Alkerwi, *Chocolate intake is associated with better cognitive function: The Maine-Syracuse Longitudinal Study.* Appetite, 2016. **100**: p. 126-32.
- 22. Solfrizzi, F.P., Coffee Consumption Habits Impact the Risk of Mild Cognitive Impairment: The Italian Longitudinal Study on Aging | Journal of Alzheimer's Disease. Journal of Alzheimers Disease, 2015.
- 23. Kent, K., et al., Consumption of anthocyanin-rich cherry juice for 12 weeks improves memory and cognition in older adults with mild-to-moderate dementia. Eur J Nutr, 2017. **56**(1): p. 333-341.
- 24. Krikorian, R., et al., *Blueberry Supplementation Improves Memory in Older Adults*. J Agric Food Chem, 2010. **58**(7): p. 3996-4000.
- 25. Eyre, H.A., et al., *A randomized controlled trial of Kundalini yoga in mild cognitive impairment*. Int Psychogeriatr, 2017. **29**(4): p. 557-567.
- 26. Ngandu, T., et al., A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. Lancet, 2015. **385**(9984): p. 2255-63.
- 27. Petrie, M., et al., *Beet Root Juice: An Ergogenic Aid for Exercise and the Aging Brain.* The Journals of Gerontology: Series A, 2017. **72**(9): p. 1284-1289.

Erectile Dysfunction (ED)

Cardiovascular disease and erectile dysfunction similar risk factors including: hypertension, hyperlipidemia, tobacco use, high cholesterol diabetes, alcohol use, obesity, age, low testosterone, low physical activity, untreated sleep apnea and stress. As men get older ED becomes more prevalent, however presence of ED in males younger than 50 is a red flag for future cardiovascular events such as heart attack or stroke.

ED as predictor of heart disease

• In a population of men age 39–69 with ED without any cardiac symptoms, 55 percent had evidence of CAD (coronary artery disease) on CT scan but only 10 percent had abnormal stress test. This suggests that ED may be a predictor of subclinical, non-flow-limiting (not yet interfering with blood flow) CAD, undetectable on exercise stress testing.[1]



Yet another reason to quit smoking

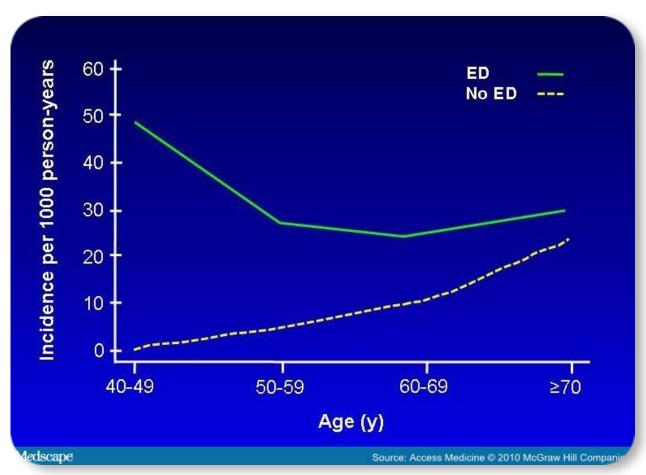
• In a 2013 meta analysis of 92,757 men, results concluded that men with ED have a 62 percent increased risk of heart attack, 39 percent increased risk of stroke and 25 percent increased risk of death compared to those without ED.[2]

Onset of ED and risk of CAD (coronary artery disease)

- ED and CAD are different manifestations of the same underlying vascular problem, but age when this problem starts makes a big difference!
- When ED occurs in a younger man (age <60) it is associated with a marked increase in the risk of future cardiac events, while it has less prognostic value in older men. While ED had little

relationship with the development of future cardiac events in men age 70 years and older, it was associated with a nearly fiftyfold increase in the 10-year incidence in men 49 years and younger! [3]





Incidence of Coronary Artery Disease with Respect to Age and Erectile Dysfunction (ED) Status. [3] (Reproduced with permission)

Drugs and ED

The list on the right also includes prescription medications which may cause ED. Do not stop taking your medications without first consulting with your doctor!

- Blood pressure medications: typically, diuretics (HCTZ, chlorthalidone), beta blockers (e atenolol, metoprolol) alpha blocker (doxazosin, prazosin). Calcium channel blockers such as amlodipine has least effect on erection.
- Antidepressants can cause ED and inability to achieve orgasm.
- Antipsychotic medications: ED seen in 45-90 percent of patients.

Alcohol
Amphetamines
Barbiturates
Cocaine
Marijuana
Methadone
Nicotine
Opiates

Sex and Cardiovascular Health

- Benzodiazepines: Used to treat anxiety, insomnia, muscle spasm, seizures. benzodiazepines lessen sexual interest, excitement and sensation, interfere with the production of testosterone, a hormone important for sexual desire in women as well as men. The sexual problems most frequently associated with benzodiazepines are diminished orgasms, pain during intercourse, ED and ejaculation problems.
- H2 Blockers. (Tagamet, Pepcid, Zantac) cause impotence (and breast enlargement in males) when taken at high doses for a long period of time.
- Anti-seizure medications such as carbamazepine (Tegretol) and phenytoin (Dilantin), less with newer medications such as gabapentin (Neurontin) and topiramate (Topamax).

Exercise and erectile function

- Moderate to vigorous aerobic exercise significantly improved erection! [4]
- Unsupervised home walking program significantly improved erectile function after heart attack!
- Patients discharged from hospital 30 days later were instructed to participate in a progressive outdoor walking program. Within 30 days of the program there was a 71 percent self reported decrease in ED with walking and 9 percent increase in ED in the non-active control group. [5]

Watching pornography may lead to ED!

In a recent study of 312 young men (without organic causes for ED), aged 20 to 40, scientists find that men who prefer pornography to real-world sexual encounters might find themselves caught in a trap. They were unable to perform sexually with other people when they have the opportunity. Porn-addicted men are more likely to suffer from erectile dysfunction. They are also less likely to be satisfied with sexual intercourse and more likely to divorce. A separate survey of 48 women found no association between pornography and sexual dysfunction, even though



about 40 percent said they also watch pornography. Pornography has a similar addiction potential of cocaine! [6]

Sleep apnea and ED

• A correlation between severe obstructive sleep apnea and ED. CPAP treatment is effective in improvement of sexual performance of these patients. [7]

Sexual Activity and its Benefits

- In a study published in 2010, men who had sex two or more times a week decreased their risk for heart disease by 45 percent. [8]
- A 2004 study including 29,342 men between the ages of 46 and 81 found that those who ejaculated 21 or more times a month from sexual intercourse, nocturnal emissions and masturbation had a 33 percent lower risk of prostate cancer. [9]



• A 2003 study including 2,338 adults showed similar results that men who ejaculated 4.6 to 7 times a week compared to less than 2.3 times a week had a 36 percent decreased risk of prostate cancer. [10]

Risk of heart attack during sex is very very small, even after heart attack. Regular exercise also was found to reduce the risk of MI by sexual activity!

- The risk of heart attack during sex is very small. For a 50-year old man who exercises regularly, his risk for a heart attack is 3 in a million per hour. For an individual recovering from a heart attack, their risk is 30 in a million per hour. [11]
- Sexual intercourse averages 2- 3 metabolic equivalents (METs) and may go up to 3-4 METs at orgasm. This is comparable to walking or climbing the stairs, which is about 2 and 3-4 METs, respectively.
- The cardiovascular benefits of sex apply only to men in monogamous relationships.
- Infidelity dramatically and sometimes fatally cancels any benefit!
- This does not even include violent death and injuries related to infidelity!
- Remember Lorena Bobbit and her unfortunate husband John? [12]



Sex and Cardiovascular Health

Treatment for ED and risk of heart disease: Good News!

• A 2017 study including 43,145 men found that those treated with phosphodiesterase-5 inhibitors (Viagra, Cialis, Levitra) after a first heart attack had a lower risk of mortality of 33 percent and a lower risk of hospitalization for heart failure of 40 percent compared to those untreated. [13]

Frequent sexual activity improves cognitive function in older adults:

Weekly sexual activity was associated with better overall cognitive function in older adults age 50-83 years old. Increased sexual activity leads to enhanced dopamine secretion which is linked to improved working memory and executive function in older adults. [14]



Sex and Cardiovascular Health

- 1. Jackson, G. and S. Padley, *Erectile dysfunction and silent coronary artery disease:* abnormal computed tomography coronary angiogram in the presence of normal exercise ECGs. Int J Clin Pract, 2008. **62**(6): p. 973-6.
- 2. Vlachopoulos, C.V., et al., *Prediction of Cardiovascular Events and All-Cause Mortality With Erectile Dysfunction*. Circulation: Cardiovascular Quality and Outcomes, 2013. **6**: p. 99-109.
- 3. Inman, B.A., et al., *A population-based, longitudinal study of erectile dysfunction and future coronary artery disease.* Mayo Clin Proc, 2009. **84**(2): p. 108-13.
- 4. Silva, A.B., et al., *Physical activity and exercise for erectile dysfunction: systematic review and meta-analysis.* Br J Sports Med, 2016.
- 5. Begot, I., et al., A home-based walking program improves erectile dysfunction in men with an acute myocardial infarction. Am J Cardiol, 2015. 115(5): p. 571-5.
- 6. Park, B.Y., et al., Is Internet Pornography Causing Sexual Dysfunctions? A Review with Clinical Reports. Behav Sci (Basel), 2016. 6(3).
- 7. Taskin, U., et al., *Erectile dysfunction in severe sleep apnea patients and response to CPAP.* Int J Impot Res, 2010. **22**(2): p. 134-9.
- 8. Hall, S.A., et al., *Sexual Activity, Erectile Dysfunction, and Incident Cardiovascular Events*. Am J Cardiol, 2010. **105**(2): p. 192-7.
- 9. Leitzmann, M.F., et al., *Ejaculation frequency and subsequent risk of prostate cancer.* Jama, 2004. **291**(13): p. 1578-86.
- 10. Giles, G.G., et al., Sexual factors and prostate cancer. BJU Int, 2003. 92(3): p. 211-6.
- 11. Muller, J.E., *Triggering of cardiac events by sexual activity: findings from a case-crossover analysis.* Am J Cardiol, 2000. **86**(2a): p. 14f-18f.
- 12. Wikipedia, John and Lorena Bobbitt Wikipedia, Wikipedia, Editor. 2017.
- 13. Andersson, D.P., et al., Association between treatment for erectile dysfunction and death or cardiovascular outcomes after myocardial infarction. Heart, 2017. **103**(16): p. 1264-1270.
- 14. Wright, H., R.A. Jenks, and N. Demeyere, *Frequent Sexual Activity Predicts Specific Cognitive Abilities in Older Adults*. J Gerontol B Psychol Sci Soc Sci, 2017.

Smoking is the second largest risk factor for disability and early death and a study published in The Lancet in 2016 found that smoking causes 1 in 10 deaths worldwide. The countries responsible for about half of these deaths include China, US, Russia and India. [1] Tobacco ruins your health and global economy! Smoking and its side effects cost the world's economies more than \$1 trillion and kill about 6 million people each year with deaths expected to rise by more than a third by 2030, according to a new report from the World Health Organization and the National Cancer Institute.



(January 2017) Those losses exceed annual global revenue from tobacco taxes, estimated to be \$269 billion in 2013-14. Less than \$1 billion was invested in tobacco control.

"The tobacco industry produces and markets products that kill millions of people prematurely, rob households of finances that could have been used for food and education, and impose

immense health care costs on families, communities and countries," Oleg Chestnov, (WHO's assistant director-general for noncommunicable diseases and mental health). [2]

When you smoke cigarettes, over 7,000 chemicals are released into the air and at least 69 of these chemicals are dangerous and are cancer causing. [3]

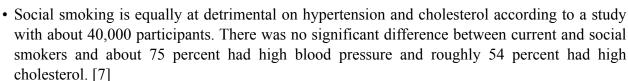


Smoking leads to		
Heart disease	Liver cancer	
Lung cancer	Bladder cancer	
Diabetes	Ectopic pregnancies	
Erectile dysfunction	Weakened bones	
Stroke	Cataracts	
COPD	Decaying teeth	
and MUCH more! [4]		



Physicians used to promote tobacco products... Smoking & Cardiovascular Disease

- Risk of cardiovascular disease increases 64 percent by smoking as few as three cigarettes a day. Risk doubles by smoking a pack a day. [5]
- Quitting smoking can reduce heart-related death rate by 23 percent. [6]



Smoking and Dementia [8]

- Risk of Alzheimer's doubles (157 percent increase) in people smoking at least two packs of cigarettes a day in their mid-life years.
- They have a 172 percent increased risk of vascular dementia, which is linked to problems in blood vessels supplying the oxygen to the brain.
- The good news for people who quit by mid-age is that their dementia risk 20 years later is the same as those who never smoked.





DNA Changes with Smoking

- A 2016 study found that those who smoked a pack of cigarettes a day had a significant amount of DNA mutations in their cells after a year.
- The results concluded that individuals who smoked a pack of cigarettes a day caused: 150 mutations in lung cells, 97 mutations in the larynx box, 23 mutations in the mouth cells, 18 mutations in the bladder and 6 in the liver after a year.
- These changes are permanent!!! [9]



Third Hand Smoking Does Exist!

- If you smoke, you are not only putting your children at risk of secondhand smoke, but also third hand smoke a study shows!
- The study completed in 2016 with 25 children found that children who live in household of smokers had high levels of nicotine on their hands compared to children in nonsmoking households.
- One child had a nicotine level of about 691ng/ wipe which is actually more than what is expected of an active smoker! [10]



What about e-cigarettes?

Former smokers who only use e-cigarettes or nicotine replacement therapy (NRT such as patch, gum) are substantially less likely to be exposed to carcinogens and toxins than those who continue to smoke, as demonstrated by a recent large cross-sectional study.

Furthermore, the data show no evidence those former smokers who use e-cigarettes exclusively



are exposed to greater levels of carcinogens or toxins than those who only use NRT, suggesting e-cigarettes are comparable to NRT in terms of long-term safety. In this particular study, investigators measured levels of multiple cancer causing chemicals including the established carcinogen 4- (methylnitrosamino)-1-(3-pyridyl)-1 butanol, or NNAL, (another proof that anything with such a long name can't be good for you) NNAL levels with e-cig users were 97 percent lower than with regular cigarette smokers! [11]

There are however some undesirable effects of vaping:

- Increased aortic stiffness (aorta is the biggest vessel in the body origination from the left ventricle of the heart) leading to in blood pressure. [12]
- Habitual e-cigarette use was associated with a shift in cardiac autonomic balance toward sympathetic predominance (fight and flight system activation) and increased oxidative stress, both associated with increased cardiovascular risk. (death, myocardial infarction) [13]

E cigarettes - the verdict:

• Safer than regular cigarettes but not harmless! It is ok to use as a tool to quit smoking but with a goal to stop vaping as well!

The Fatal Toll of Cheap Cigarettes

A 2017 study suggests that the availability of cheaper, off-brand cigarettes is associated with an increase in infant mortality.

Researchers studied the link between cigarette prices and infant mortality in 23 European countries from 2004 through 2014. During this time, there were more than 53 million live births. After controlling for other factors, they found that



a \$1.18 increase in average price per pack was associated with a decline of 230 deaths per 1 million babies in the first year of life and 160 deaths per 1 million babies in the second year.

But when a cheap enough brand was available, the number of infant deaths increased. A 10 percent difference between the median price and the price of an off-brand bargain pack was associated with an increase of 70 deaths per 1 million live births, the researchers found.

Increases in average price between 2004 and 2014, which generally followed increases in tobacco taxes, were associated with 9,208 fewer infant deaths. But if there had been no bargain cigarettes available, 3,195 more deaths could have been avoided.

"Tobacco companies can load price increases onto premium brands and sell cheaper cigarettes at a loss so that poor people and young people can still take up smoking," said the lead author, Filippos Filippidis, at Imperial College London. [14]

I could not resist and took a picture of this poster hanging in the window of a gas station in rural Indiana. It is signed by "Citizens for Tobacco Rights" Guess who are they? Philip Morris, a company concerned only with profits!

Marijuana and The Heart.

We regret to report: not good...

 A recent 2016 study, published in the journal Nature, found that cannabis use depresses the dopamine reward system.
 Dopamine is involved in processing motivation, pleasure and reward. Long-term and excessive cannabis use can decrease the amount of dopamine released and cause negative emotions, which can lead to mental illness. [15]



- Smoking marijuana causes increases in heart rate that can last 2-3 hours after stopping smoking. Sinus arrhythmias, premature ventricular contractions and atrial fibrillations are independently associated with marijuana use. [16]
- Marijuana effects cardiovascular health by increasing systolic and diastolic blood pressure, angina, and risk for heart attack.
- In a study with about 3,900 participants, authors concluded that risk for a heart attack an hour after marijuana use is increased 4.8 times.
- For those who have had a heart attack and still use marijuana more than once a week, the risk for mortality is increased threefold.

• The time to angina while exercising decreases by 48 percent after smoking marijuana once for people with chronic stable angina. [17]

• Marijuana use increases the risk of Takotsubo syndrome, also called stress cardiomyopathy two-fold. This disease causes the left ventricle to swell and causes left ventricular dysfunction. Patients who smoke marijuana and have Takotsubo syndrome have a higher risk of cardiac arrest and getting an ICD than nonusers. 2.4 percent vs. 8 percent and 2.4 percent vs. percent respectively. [18]

Marijuana use holds three-fold blood pressure death risk

In a retrospective follow-up study of 1,213 people aged 20 or above, scientists discovered that people who smoke marijuana have a three times greater risk of dying from hypertension, or high blood pressure, than those who have never used the drug. The average duration of use among users of marijuana, or cannabis, was 11.5 years. The results showed marijuana users had a 3.42-times higher risk of death from hypertension than non-users, and a 1.04 greater risk for each year of use. [19]



- 1. Marissa B Reitsma, N.F., Marie Ng, Joseph S Salama, et al, *Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the Global Burden of Disease Study 2015*, in *Lancet.* 2017. p. 1885-906.
- 2. Institute, N.C. NCI Tobacco Control Monograph Series 21. 2017.
- 3. Association, A.L., What's In a Cigarette? American Lung Association, 2017.
- 4. Health, C.s.O.o.S.a., *Smoking and Tobacco Use; Fact Sheet; Health Effects of Cigarette Smoking.* Center for Disease Control and Prevention, 2017.
- 5. Pope, C.A., 3rd, et al., Cardiovascular mortality and exposure to airborne fine particulate matter and cigarette smoke: shape of the exposure-response relationship. Circulation, 2009. **120**(11): p. 941-8.
- 6. Brunner, E., *Risk factors raised by socioeconomic deprivation that doctors can manage*, in *EAS Congress*. 2010: Hamburg, Germany.
- 7. Gawlik, K.S., B.M. Melnyk, and A. Tan, *An Epidemiological Study of Population Health Reveals Social Smoking as a Major Cardiovascular Risk Factor.* Am J Health Promot, 2017: p. 890117117706420.
- 8. Rusanen, M., et al., *Heavy smoking in midlife and long-term risk of Alzheimer disease and vascular dementia*. Arch Intern Med, 2011. **171**(4): p. 333-9.
- 9. Alexandrov, L.B., et al., *Mutational signatures associated with tobacco smoking in human cancer.* Science, 2016. **354**(6312): p. 618-622.
- 10. Mahabee-Gittens, E.M., A.L. Merianos, and G.E. Matt, *Preliminary evidence that high levels of nicotine on children's hands may contribute to overall tobacco smoke exposure*. Tob Control, 2017.
- 11. Shahab, L., et al., *Nicotine, Carcinogen, and Toxin Exposure in Long-Term E-Cigarette and Nicotine Replacement Therapy Users: A Cross-sectional Study.* Ann Intern Med, 2017. **166**(6): p. 390-400.

- 12. Vlachopoulos, C., et al., *Electronic Cigarette Smoking Increases Aortic Stiffness and Blood Pressure in Young Smokers*. J Am Coll Cardiol, 2016. **67**(23): p. 2802-3.
- 13. Moheimani, R.S., et al., *Increased Cardiac Sympathetic Activity and Oxidative Stress in Habitual Electronic Cigarette Users: Implications for Cardiovascular Risk.* JAMA Cardiology, 2017. **2**(3): p. 278-284.
- 14. Filippidis, F.T., et al., Association of Cigarette Price Differentials With Infant Mortality in 23 European Union Countries. JAMA Pediatrics, 2017.
- 15. Bloomfield, M.A.P., et al., *The effects of Δ9-tetrahydrocannabinol on the dopamine system.* Nature, 2016. **539**: p. 369-377.
- 16. Korantzopoulos, P., et al., *Atrial fibrillation and marijuana smoking*. Int J Clin Pract, 2008. **62**(2): p. 308-13.
- 17. Joe Kattoor, J.M., Marijuana and Coronary Heart Disease American College of Cardiology. JACC, 2016.
- 18. Busko, M., Marijuana Use Can Double Risk of Takotsubo Cardiomyopathy, in American Heart Association Scientific Sessions. 2016, @Medscape: New Orleans, LA.
- 19. Yankey, B., Marijuana associated with three-fold risk of death from hypertension. Science Daily, 2017.

Why Vaccination Matters

Influenza vaccination

Myocardial infarction

There is a large body of observational and clinical trial evidence that shows that influenza vaccine protects against acute heart attack. Estimates of the efficacy of influenza vaccine in preventing heart attack range from 15 percent to 45 percent. This is a similar range of efficacy compared with the accepted routine coronary prevention measures such as smoking cessation (32-43%),



statins (19-30%) and antihypertensive therapy (17-25%). [1]

Atrial fibrillation

In a study of 57000 individuals influenza vaccination was associated with 18 percent decrease in diagnosis of new atrial fibrillation! [2]

Congestive heart failure

In a study of 8000 patients with chronic congestive heart failure influenza vaccination was associated with almost 20 percent reduction in risk of death! [3]

Stroke

Study of near 18,000 patient's evaluated risk of stroke depending on flu vaccinations status Flu vaccines administered earlier in the flu season offered greater protection. In the first week after the jab, there were 36 per cent fewer cases of stroke than would be otherwise expected among a 'baseline' population, while the second week showed a 30 percent reduction. The third and fourth weeks saw 24 percent fewer stroke cases, dropping to 17 percent between 29 days and 59 days after the jab. [4] Subsequent review of previously published data confirmed significant effect of flu vaccination on stroke prevention. [5]

And be really happy when you get a flu shot!

In older adults aged 65 to 85 years old (who often fail to respond to flu vaccine) Greater levels of positive mood on the day of vaccination were associated with higher blood levels of antibodies to H1N1, a potentially dangerous flu strain, at both four and 16 weeks post-vaccination. No other factors measured were associated with improved immune response. When we are stressed, angry and depressed, cortisol (chronic stress hormone) levels are high, which in turn suppressed immune system! [6]



Why Vaccination Matters

O, the Joy of Shingles

It is not just the pain....

However some time the pain can be so intense that death from heart attack may seem as a relief!

In a study of 519,880 patients, newly diagnosed herpes zoster (HZ) significantly raised the risks of stroke and MI in the first year after infection. Perhaps more surprisingly, the risks were especially high in those under 40 years of age, a group that typically has fewer atherosclerosis risk factors. Risk of stroke increased by 35 percent and MI (heart attack) by 59 percent! The risks of stroke and MI were highest in the first year after HZ (herpes zoster) infection and tended to decrease with time. [7]



- 1. MacIntyre, C.R., et al., *Influenza vaccine as a coronary intervention for prevention of myocardial infarction*. Heart, 2016. **102**(24): p. 1953-1956.
- 2. Chang, T.Y., et al., *The association between influenza infection, vaccination, and atrial fibrillation: A nationwide case-control study.* Heart Rhythm, 2016. **13**(6): p. 1189-94.
- 3. Vardeny, O., et al., *Influenza Vaccination in Patients With Chronic Heart Failure: The PARADIGM-HF Trial.* JACC Heart Fail, 2016. **4**(2): p. 152-158.
- 4. Asghar, Z., C. Coupland, and N. Siriwardena, *Influenza vaccination and risk of stroke: Self-controlled case-series study.* Vaccine, 2015. **33**(41): p. 5458-63.
- 5. Lee, K.R., et al., *Effect of Influenza Vaccination on Risk of Stroke: A Systematic Review and Meta-Analysis*. Neuroepidemiology, 2017. **48**(3-4): p. 103-110.
- 6. Ayling, K., et al., *Positive mood on the day of influenza vaccination predicts vaccine effectiveness: A prospective observational cohort study.* Brain Behav Immun, 2017.
- 7. Kim, M.C., et al., *Herpes Zoster Increases the Risk of Stroke and Myocardial Infarction*. J Am Coll Cardiol, 2017. **70**(2): p. 295-296.

City of Cincinnati by neighborhood: there is a 21.4 years difference in life expectancy depending on where you live.

U.S. Life Expectancy Varies by Two Decades Depending on Location (not different than City of Cincinnati)

- Nationwide in 2014, the average life expectancy was about 79.1 years, up 5.3 years from 1980.
- For men, life expectancy climbed from 70 years to 76.7 years, while for women it increased from 77.5 years to 81.5 years.
- There are stark disparities: a baby born in Oglala Lakota County, South Dakota, can expect to live just 66.8 years, while a child born in Summit County, Colorado, can expect to live 86.8 years, on average.
- Risk factors obesity, lack of exercise, smoking, hypertension, and diabetes explained 74 percent of the variation in longevity in the U.S.
- Socioeconomic factors a combination of poverty, income, education, unemployment and race were independently related to 60 percent of the inequality, and access to and quality of health care explained 27 percent.
- Several counties in South and North Dakota, typically with Native American reservations, had the lowest life expectancy.

Cincinnati neighborhoods with lowest life expectancy	Years
South Fairmount	66.4
Lower Price Hill	66.8
Sedamsville/Riverside	67.0
Camp Washington	67.8
Avondale	68.2

Cincinnati neighborhoods with highest life expectancy	Years
Mt. Washington	82.9
Madisonville	83.1
Hyde Park	83.2
Mt. Lookout	85.9
Mt. Adams	86.4
North Avondale/Paddock Hills	87.1
Mt. Lookout/Columbia Tusculum	87.8



- Counties along the lower half of the Mississippi and in eastern Kentucky and southwestern West Virginia also had very low life expectancy compared with the rest of the country.
- In contrast, counties in central Colorado had the highest life expectancy. Some of the biggest gains in life expectancy comparing to data from 1980 were seen in counties in central Colorado, Alaska and in metropolitan areas around San Francisco and New York.
- There was almost no improvement in life expectancy in some southern counties in states stretching from Oklahoma to West Virginia. Many counties where life expectancy dropped, the most are in Kentucky. [1]

LOW INCOME

EDUCATION

CAREER

Income, Education and your Heart

- The Atherosclerosis Risk in Communities (ARIC) is a study initiated in 1987 with 10-years follow-up of 15,495 adults aged 45-64 years in four Southern and Mid-Western communities.
- Participants reported their education and income levels in 1987, and then over the course of 10 years were periodically evaluated for heart-disease diagnoses and changes in their risk factors, including cholesterol, blood pressure and smoking.
- The results indicated that people with lower socioeconomic status had a 50 percent greater risk of developing heart disease than other study participants although it is known that people with low socioeconomic status have a greater risk for developing heart disease and other health problems.
- The reason is often attributed to reduced health-care access or poor adherence to treatments such as smoking cessation or medication.
- This study showed for the first time that the increased risk endured despite long-term improvements in other risk factors, indicating that access and adherence could not account for the differences. Low socioeconomic status is a heart-disease risk factor alone and needs to be regarded as such by the medical community! [2]

Level of education and risk of heart disease:

Level of education appears to be associated with the odds for heart disease. 2017 study reviewed data from nearly 14,000 white and black Americans who were followed from 1987 through 2013. In men, the risk of cardiovascular disease (which included coronary heart disease, heart failure and stroke) between ages 45 to 85 ranged from 59 percent for those with a grade school education, to 42 percent for those who'd earned a



graduate degree, whereas for women, almost 51 percent of those with a grade school education had heart disease, compared to just 28 percent of those who'd completed graduate school. Of interest, income did not change this association. [3]

Unemployment, job loss may increase risk of stroke mortality, morbidity

- This large analysis examined 21,902 Japanese men and 19,826 Japanese women who enrolled in the Japan Public Health Center-based prospective study from 1990 to 1993 at nine public health centers in Japan. The follow up was 15 years.
- Compared with continuously employed participants, there was up 58 percent increase in risk of stroke for men who lost their jobs and up 51 percent for women who lost their jobs. For mortality, the risk was 122 and 148 percent respectively.



- For re-employed men, the risk for stroke was 196 percent and 321 percent for mortality. For re-employed women, the risk for stroke and mortality was 30 percent and 28 percent, respectively.
- For continuously unemployed men risk was 36 percent for stroke incidence and 424 percent for mortality. For continuously employed women, risk was 58 percent for stroke incidence and 435 percent for mortality.
- For men who experienced at least one spell of unemployment, the risk was 76 percent for stroke incidence and 200 percent for mortality. For women who experienced at least one spell of unemployment, the risk was up 38 percent for stroke incidence and 98 percent for mortality.
- For men and women, having at least one spell of unemployment also was associated with an increased risk of hemorrhagic and ischemic stroke. [4]

The Message: Job security during the most productive work ages could help reduce stroke risk!

Food insecurity as risk factor for heart disease:

- Food insecurity refers to the inability to afford enough (healthy) food for an active, healthy life.
- Numerous studies have shown associations between food insecurity and adverse health outcomes among children and adults. It is linked to high blood pressure, diabetes and high cholesterol. Almost 50 millions American are food insecure. [5], [6]
- Food insecurity during pregnancy leads to higher weight gain, high blood pressure and gestational diabetes. [7]



Childhood poverty and risk of heart failure as adult:

Scientist evaluated 1871 participants who reported family socioeconomic status at ages 3 to 18 years and were evaluated for LV structure and function 31 years later and discovered that childhood poverty lead to stiffening of heart muscle (diastolic heart failure) in adults, effect which was independent from obesity, high blood pressure and smoking! [8]



Homelessness and heart disease:

- Homeless people with mental illness are at high risk for heart disease. There was 24.5 percent risk of heart attack, fatal or nonfatal stroke, or sudden cardiac death over 30 years compared to 10 percent for a person of the same age and gender without history of tobacco use, hypertension, diabetes, obesity.
- The risk of cardiovascular disease in homeless people with mental illness was highest among men and those with substance abuse disorders, even in absence of typical risk factors such as diabetes or hypertension.
- This risk is partially related to smoking: as many as 90 percent of people with schizophrenia and bipolar disorder smoke, as do about 70 percent of people with a major depressive disorder.
- The smoking rate in the general population is about 20 percent (Canada). [9]

Do something about it and help people in need: volunteer!

"The essence of life is too serve others and do good" - Aristotle

When you volunteer, you are also the winner:

- Volunteering not only has a powerful effect on your mood by becoming more altruistic and reducing negative thoughts but has measurable effects on our bodies.
- In a large study of 10th graders, volunteering significantly reduced cholesterol levels, suppressed inflammation (measured by level of a molecule called interleukin 6 or IL-6), and significantly recued BMI (body mass index). [10]
- Adults over age 50 who volunteered on a regular basis were less likely to develop high blood

pressure than non-volunteers. And high blood pressure is an important indicator of future complications as it contributes to heart and kidney disease, stroke, and premature death.

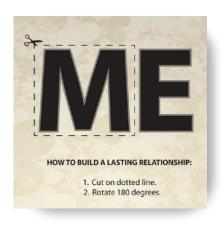


How much time would one need to put into volunteer work to lower your blood pressure or live longer?

• In the Carnegie Mellon study, 200 hours of volunteering per year correlated to lower blood pressure. Other studies have found a health benefit from as little as 100 hours of volunteering a year. There is no research on type of volunteering and degree of benefit. [11]

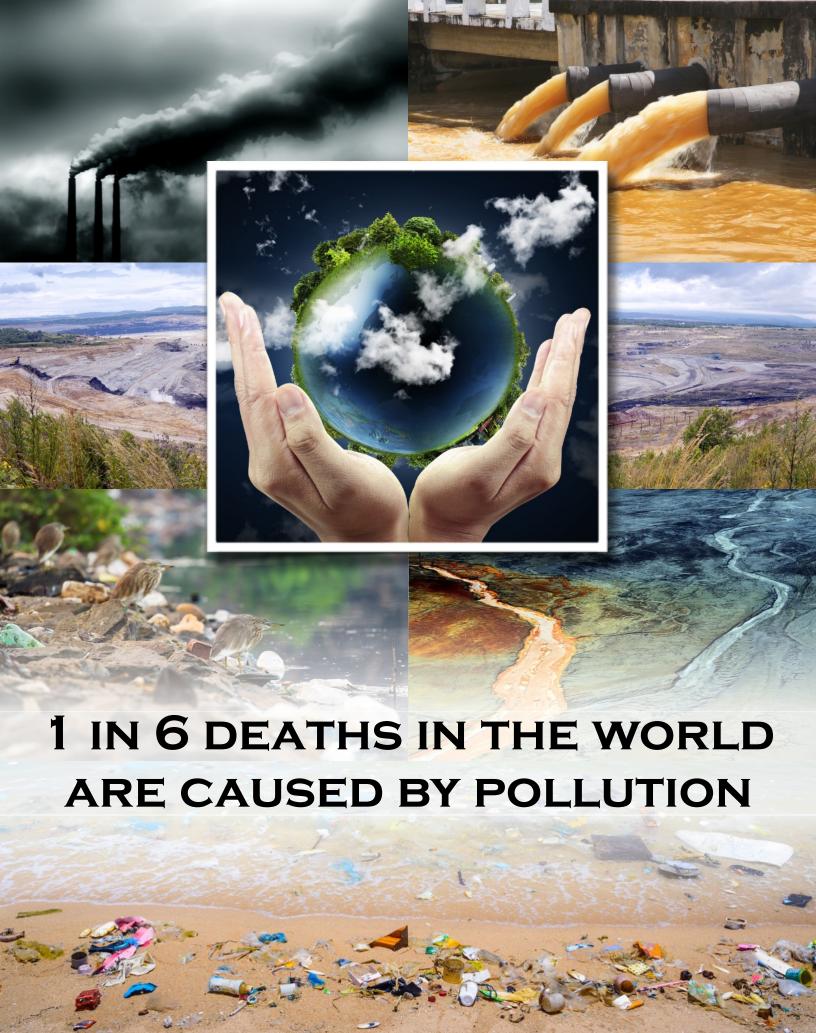
The key for deriving health benefits from volunteering is to do it for the right reasons:

• Individuals who volunteered on regular basis lived longer, but only if their intentions were truly altruistic. In other words, they had to be volunteering to help others, not to just make themselves feel better! [12]





- 1. Dwyer-Lindgren, L., et al., *Inequalities in Life Expectancy Among US Counties, 1980 to 2014: Temporal Trends and Key Drivers.* JAMA Internal Medicine, 2017. **177**(7): p. 1003-1011.
- 2. Franks, P., et al., *Do changes in traditional coronary heart disease risk factors over time explain the association between socio-economic status and coronary heart disease?* BMC Cardiovascular Disorders, 2011. **11**(1): p. 28.
- 3. Kubota, Y., et al., Association of Educational Attainment With Lifetime Risk of Cardiovascular Disease: The Atherosclerosis Risk in Communities Study. JAMA Internal Medicine, 2017. 177(8): p. 1165-1172.
- 4. Eshak, E.S., et al., *Changes in the Employment Status and Risk of Stroke and Stroke Types*. Stroke, 2017. **48**(5): p. 1176-1182.
- 5. Gundersen, C. and J.P. Ziliak, Food Insecurity And Health Outcomes. Health Affairs, 2015.
- 6. Seligman, H.K., B.A. Laraia, and M.B. Kushel, *Food Insecurity Is Associated with Chronic Disease among Low-Income NHANES Participants12*, in *J Nutr.* 2010. p. 304-10.
- 7. Laraia, B.A., A.M. Siega-Riz, and C. Gundersen, *Household food insecurity is associated with self-reported pregravid weight status, gestational weight gain, and pregnancy complications.* J Am Diet Assoc, 2010. **110**(5): p. 692-701.
- 8. Laitinen, T.T., et al., Association of Socioeconomic Status in Childhood With Left Ventricular Structure and Diastolic Function in Adulthood: The Cardiovascular Risk in Young Finns Study. JAMA Pediatrics, 2017. **171**(8): p. 781-787.
- 9. Gozdzik, A., et al., *Cardiovascular risk factors and 30-year cardiovascular risk in homeless adults with mental illness.* BMC Public Health, 2015. **15**(1): p. 165.
- 10. Schreier, H.M., K.A. Schonert-Reichl, and E. Chen, *Effect of volunteering on risk factors for cardiovascular disease in adolescents: a randomized controlled trial.* JAMA Pediatr, 2013. **167**(4): p. 327-32.
- 11. Sneed, R.S. and S. Cohen, *A prospective study of volunteerism and hypertension risk in older adults*. Psychol Aging, 2013. **28**(2): p. 578-86.
- 12. Konrath, S., et al., *Motives for volunteering are associated with mortality risk in older adults.* Health Psychol, 2012. **31**(1): p. 87-96.



The air you breathe and cardiovascular disease

- Air pollution kills 3.3 million people a year and is expected to kill 6.6 million worldwide by 2050. [1]
- Increases risk of stroke, coronary artery disease, COPD.
- Linked to autism and anxiety.
- Patients exposed to PT2.5 (fine particulate matter) at concentrations at 2.5 mcg/m3 typically seen large metropolitan areas had 46 percent increase in silent strokes and brain

volume reduction corresponding to 1 year of aging. [2]



A growing body of research indicates strokes among U.S. millennials ages 18 to 34 have soared in recent years. West and Midwest have seen especially worrisome increases among younger adults. Moreover, large cities appear to have seen bigger increases than rural areas. Researchers at the U.S. Centers for Disease Control and Prevention concluded that in a nine-year span from 2003 to 2012 there was a 32 percent spike in strokes among 18 to 34 year old women and a 15 percent increase for



men in the same range. There was a significant regional variation. In western cities with more than one million residents, for example, the analysis found strokes increased about 85 percent during the 2003 to 2012-time period. In the West as a region, strokes rose 70 percent at the same time. Across the Midwest they increased 34 percent. But in the South the relative increase was smaller and, unlike the spikes in other mentioned areas, this jump did not appear to be statistically significant. Pollution is a contributing factor, which explaining the higher rates in urban settings. [3]

Air pollution and risk of heart attack

Long term exposure (average 30 years) increased risk of fatal heart attack by 51 percent. [4]

A study form Shanghai China demonstrated that even short-term exposure to moderate-heavy pollution increased risk of heart attack by 16 percent! [5]



Air pollution and HDL

Adults who live in areas especially beset by air pollution, particularly from automobile traffic, tend to have lower HDL-cholesterol levels and lower HDL particle numbers, explaining why poor air quality promotes plaque buildup. The effect was proportional to levels of $PM_{2.5}$, which is solid and liquid matter smaller than 2.5 μ m in diameter and is a measure of air pollution. [6]

Pollution and your kidneys

A large study published in September 2107 followed 2,482,737 veterans for an average of eight and a half years.

Using data on air pollution from NASA and the Environmental Protection Agency, (when it still existed!) the researchers found that increases in PM 2.5 corresponded directly worsening kidney function. PM 2.5 particles are small enough to enter the bloodstream where they make their way to the kidneys, which are especially prone to injury from pollutants.

The scientists calculated that "unhealthy" pollution levels lead to an annual increase of 44,793 cases of chronic kidney disease, and 2,438 cases of end-stage kidney disease requiring dialysis. Even levels below those considered "safe" increased risk of kidney failure! [7]



Patient undergoing dialysis

- 1. Lelieveld, J., et al., *The contribution of outdoor air pollution sources to premature mortality on a global scale*. Nature, 2015. **525**: p. 367-371.
- 2. Wilker, E.H., et al., Long-term exposure to fine particulate matter, residential proximity to major roads and measures of brain structure. Stroke, 2015. **46**(5): p. 1161-6.
- 3. George, M.G., et al., *Prevalence of Cardiovascular Risk Factors and Strokes in Younger Adults*. JAMA Neurology, 2017. **74**(6): p. 695-703.
- 4. Rosenlund, M., et al., *Long-term exposure to urban air pollution and myocardial infarction*. Epidemiology, 2006. **17**(4): p. 383-90.
- 5. Wang, X.D., et al., Short-term effects of air pollution on acute myocardial infarctions in Shanghai, China, 2013–2014, in J Geriatr Cardiol. 2016. p. 132-7.
- 6. Bell, G., et al., Association of Air Pollution Exposures With High-Density Lipoprotein Cholesterol and Particle Number. Arteriosclerosis, Thrombosis, and Vascular Biology, 2017.
- 7. Bowe, B., et al., Particulate Matter Air Pollution and the Risk of Incident CKD and Progression to ESRD. J Am Soc Nephrol, 2017.



AND DIE EARLY!

People who keep especially long hours at work, 55 h/week or more, have about a 40 percent increased long-term risk of developing atrial fibrillation (AF) compared with working 35 to 40 h/week, suggest patient-level data from more than 85,000 people across eight European observational cohorts. Importantly, the mean age in the combined cohorts was a young 43 years! Fewer than 1 percent had cardiovascular disease (CVD) at the start. All participants had been free of AF at the beginning, and the analysis adjusted for a range of socioeconomic and lifestyle AF risk factors, including age, sex, smoking, exercise level, and alcohol intake. [1]

The longer hours you work the less likely you will see retirement

Researchers from the University of Texas followed a representative sample of 1,926 initially healthy American workers for 25 years. They found a dose-response relationship between average hours worked per week for at least 10 years and increasing risk of heart attack, stroke, hypertension, angina, and other cardiovascular events.

Work and Your Heart

Compared to working 45 hours per week, working more increases your risk - see chart.

Work stress is as bad as secondhand smoke:

• In a meta-analysis of 228 scientific studies, researchers discovered that the presence of workplace stressors predicted negative health outcomes almost as well as exposure to secondhand smoke does. The study found work-family conflict more than doubled the likelihood that employees will experience self-

Hours per Week	Higher Risk
55	16%
60	35%
65	52%
70	74%
75 - double the risk! [2]	100%

reported mental health problems and increased the risk of physical health problems by more than 90 percent. Job insecurity also correlated with an increase in self-reported physical problems. A sense of low organizational justice (defined as "a lack of perceived fairness in the organization"), increased the odds of having a physician-diagnosed condition by about 50 percent, significantly more than secondhand smoke exposure.

It is estimated that more than 120,000 deaths per year and annual cost to healthcare system of \$180 billion are related to workforce stress! [3]

Solution: Either Quit or change your attitude to work!

Good news: if you enjoy your work and is not a source of continuous stress you will live longer and happier life! (Life with Purpose - see Chapter 4)

- 1. Kivimäki, M., et al., *Long working hours as a risk factor for atrial fibrillation: a multi-cohort study.* European Heart Journal, 2017. **38**(34): p. 2621-2628.
- 2. Conway, S.H., et al., Dose-Response Relation Between Work Hours and Cardiovascular Disease Risk: Findings From the Panel Study of Income Dynamics. J Occup Environ Med, 2016. 58(3): p. 221-6.
- 3. Goh, J., J. Pfeffer, and S.A. Zenios, *The Relationship Between Workplace Stressors and Mortality and Health Costs in the United States*. Management Science, 2015: p. 608-628.



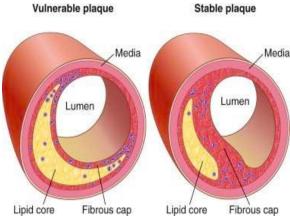
Understanding Coronary Artery Disease

There are two types of plaques present in the coronary vessels, stable and unstable (vulnerable).

Stable plaque (which is typically calcified), as it occupies more lumen eventually will interfere with blood flow with exertion and result in angina (chest pain with exertion) or shortness of breath during exercise. Even blockages, which are over 90 percent, do not interfere with blood flow at rest!

Unstable plaque (typically a soft plaque) on the other hand can rupture, leading to clot formation on the surface of the plaque, rapidly interrupting blood fowl to heart muscle. This interrupts vital oxygen delivery and results in heart attack (myocardial infarction).

The thinner the fibrous cap, the bigger the lipid core (semiliquid fat in the plaque) the unstable is the plaque (the more likely to rupture).



The right image represents plaque rupture with a thrombus formation. When plaque ruptures, semiliquid fat becomes exposed to circulating blood and our body responds the same way as it would to a cut: make a clot!

What causes plaque rupture?

- Exercise, typically in patients who are not physically active.
- Anger
- Inflammation (typically triggered by flu!)
- Systemic inflammation attracts inflammatory cells into the plaque cover (fibrous cap).

Those cells in turn to digest it secreting enzymes called metalloproteinase bleeding inside the plaque. Chemicals released inside a plaque attract tiny vessels called vasa vasorum (vessel of an vessel) which are very fragile, when one of those vessels ruptures there is extra blood in the plaque which expands in size rapidly and sometimes rupture.

Aggressive lipid lowering therapy (statins, new agents such as Repatha or Pralulent, discussed at more details in the Cholesterol chapter) decrease lipid content of the plaque making it more stable. In case of statin, plaque fats are replaced with calcium. Plant based as well Mediterranean diet has a similar effect.

Understanding Coronary Artery Disease

In a study utilizing cardiac CT, patients underwent CT scans 2 years apart. And plaque volume was measured. Patients with LDL-C below 70 mg/dl displayed a significant attenuation in plaque progression as compared with those with follow-up LDL-C levels \geq 70 mg/dl (12.7 \pm 38.2 mm³ vs. 44.2 ± 73.6 mm³, respectively. [1]

Plaque Stabilization/Regression Unstable plaque Fibrous cap Fibro

Reproduced with permission

References:

1. Shin, S., et al., *Impact of Intensive LDL*Cholesterol Lowering on Coronary Artery

Atherosclerosis Progression: A Serial CT

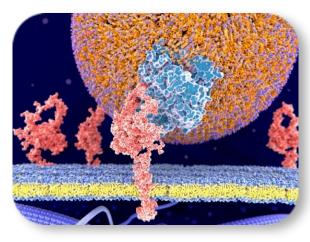
Angiography Study. JACC Cardiovasc Imaging, 2017. **10**(4): p. 437-446.

LDL

Image on right: LDL particle captured by a receptor on a surface of a hepatocyte (liver cell).

Statin denial: an Internet-driven cult with deadly consequences [1]

There is a widespread misinformation on the internet regarding statins similar to the antivaccination movement, which is groundless ("alternative facts" and "fake news"). Just



reading this information increases your risk of side effects which is classic nocebo effect.

Stopping statin after heart attack significantly increases your risk of death and recurrent heart attack!

The choice is yours!

The benefits of statins are very well established and in general life style modification alone will not be as effective as high intensity statin drug, which is very important in patients with already established coronary artery disease or diabetes (high risk group). If you are statin intolerant (after trying it again, see below) there are life style intervention (which you should follow anyway) leading to reduction of cholesterol.

Recent research shows that nearly 30 percent of patients did not receive a statin prescription after experiencing side effect, but those who continued on therapy had a 10 percent to 20 percent lower risk of cardiovascular events and death. Only 27 percent patient had side effects when a second statin was prescribed! [2]

Benefits versus risk of statin:

The absolute benefits of statin therapy depend on an individual's absolute risk of occlusive vascular events and the absolute reduction in LDL cholesterol that is achieved. For example, lowering LDL cholesterol by around 77 mg/dL) with an effective statin regimen such as atorvastatin (Lipitor) 40 mg for 5 years in 10,000 patients would typically prevent major vascular events from occurring in about 1000 patients (ie,10% absolute benefit) with pre-existing occlusive vascular disease (primary prevention: previous heart attack, stents, bypasses etc.) and in 500 patients (ie, 5% absolute benefit) who are at increased risk but have not yet had a vascular event (primary prevention). Statin therapy has been shown to reduce vascular disease risk during each year it continues to be taken, so larger absolute benefits would accrue with more prolonged therapy, and these benefits persist long term. (even in patients who took statin for 5 years and then stopped it, benefit persisted for 20 years)! The only serious adverse events (side effects) that have been shown to be caused by long-term statin therapy are myopathy (defined as muscle pain

or weakness combined with large increases in blood concentrations of creatine kinase), newonset diabetes mellitus, and, probably, hemorrhagic stroke. Typically, treatment of 10,000 patients for 5 years with high intensity statin would cause about 5 cases of myopathy (one of which might progress, if the statin therapy is not stopped, to the more severe condition of rhabdomyolysis), 50–100 new cases of diabetes, and 5–10 hemorrhagic strokes. [3]

Statin therapy and muscle pain:

Statin therapy may cause symptomatic adverse events (eg, muscle pain or weakness) in up to about 50–100 patients (ie, 0·5–1·0% absolute harm) per 10,000 treated for 5 years. However, placebo-controlled randomized trials have shown definitively that almost all of the symptomatic adverse events that are attributed to statin therapy in routine practice are not actually caused by it. Most recent research demonstrated that patients unaware that they are taking statins do not complain of muscle pains. But the same patients, once told that the drug they are taking is a statin, are much more likely to report such symptoms (this is known as nocebo effect, opposite to placebo). [4]

If you are older than 40 with high cholesterol and other risk factors consider getting coronary calcium score to see if you are going to benefit. You will receive in the report 2 numbers: one is the actual score, the other one is percentile telling you where you are among your peers of the same age, race and sex; for example, if you are in the 95th percentile, this is not necessarily a great news: it means that among your group only 5 percent will have more calcium buildup than you! (To calculate your percentile yourself go to: https://www.mesa-nhlbi.org/calcium/input.aspx.)

To prevent one cardiovascular event (death, stroke, heart attack), the predicted 5-year NNT (meaning total number of patients receiving treatment for one of them to benefit) with a statin combined with your calcium score is as follow 549 for a calcium score of 0, (1 patient will benefit, 548 will not) 94 for scores of 1–100, and (1 patient will benefit, 93 will not) 24 for scores above 100. (1 patient will benefit, 23 will not)

So based on the above numbers, if you calcium score is zero you are much more likely to experience side effect than benefits, but when calcium score exceeds 100, you are much more likely to benefit than to be harmed. [5]

On the basis of current guidelines from both NCEP and ACC/AHA:

- CAC (coronary calcium score) scores < 75th percentile *and* < 300 are to be treated with low- to moderate-dose statins.
- CAC scores > 75th percentile $or \ge 300$ are to be treated with high-dose statins.
- CAC score of zero should be considered for lifestyle modification, unless a compelling indication for statin already exists.

Aspirin NNT versus NNH (number needed to harm: total number of patients taking medications for one of them to experience side effect) As for aspirin, in the MESA study, individuals with CAC scores ≥ 100 had an estimated net benefit from aspirin regardless of their traditional risk status. (NNT = 92; estimated 5-year number needed to harm [NNH] = 442 for a major bleed). Conversely, individuals with a score of zero were unlikely to benefit (5-year NNT = 2036 for individuals with a Framingham risk score [FRS] < 10% and 808 for FRS \geq 10%; 5-year NNH = 442 for a major bleed). [6]

Non-pharmacologic treatment of elevated cholesterol:

Exercise:

- Moderate exercise decreased LDL by 10 percent and increased HDL by 3-6 percent.
- Lipoprotein particle size. Research have demonstrated that exercise can change how your LDL (bad cholesterol) behaves. Smaller lipoproteins, such as small, dense LDL, have been associated with contributing to cardiovascular disease, but having larger LDL particles does not carry this same risk. Studies have shown that moderate exercise can increase the size of your LDL particles, which can help to reduce your risk of developing cardiovascular disease. 12-week endurance exercise program reduced small, dense LDL by up to 17 percent. [7]
- Reverse cholesterol transport. A few studies in mice have suggested that exercise can enhance the transport of cholesterol from the bloodstream to the liver, where it will eventually be filtered out of the body. [8]
- **Absorption.** A few studies have shown that eight to 12 weeks of endurance exercise may slightly reduce the absorption of cholesterol from the small intestine into the bloodstream. Cholesterol production by the liver does not appear to be affected by exercise. [9]

Diet and Cholesterol:

• Plant based diet:

High fiber, very low fat, vegan diet had statin like effect on cholesterol level and resulted in 37 percent reduction in LDL! [10]

• Dietary Portfolio:

Combination of 50 g of nuts, 50 g of soy protein (soy milk, tofu, soy meat substitutes), 20 g of viscous fiber (rich sources of viscous fiber include asparagus, Brussels sprouts, sweet potatoes, turnips, apricots, mangoes, oranges, legumes, barley and oat bran) and 2 g of plant sterols (best source: Benecol spread, 4 table spoons a day) reduced LDL cholesterol by 14 percent or 26 mg/dl. [11]



Probiotic and Red Rice Yeast Combo:

Supplementation with the probiotic *Bifidobacterium longum* BB536 added to red yeast rice (extract improves lipid profiles in patients with moderate hypercholesterolemia. LDL cholesterol dropped 26 percent from 183 to 136 mg/dL after 12 weeks of supplementation vs no change with placebo. Total cholesterol declined 17 percent vs 0 percent with placebo. The changes were already achieved after just 6 weeks. Recommended dose of red rice yeast is between 1200-2400 mg a day. There were no side effects in this small study but keep in mind; main active ingredient of red yeast rice is lovastatin, which is a statin![12]

Other dietary approaches were discussed in Chapter 2 - Diet: "You are what you eat."

- Flaxseed: LDL reduction up to 15 percent was reported (30 g of milled seed s a day).
- Avocado: LDL reduction up to 20 percent (1 fruit a day).
- Almonds: LDL reduction of 10 percent when consuming 2 oz (73 g) a day.
- Soy products: modest LDL reduction of 3.5 percent.
- **Oatmeal:** (or psyllium fiber) combined with statin may double it effect without increasing risk of side effects.
- Whey protein: LDL reduction by 9 percent and change of LDL particle size form small (toxic) to large (benign). 27 g (1 oz.) of protein supplement was used per day. [13]
- Mediterranean diet: 10 percent LDL reduction in 12 weeks, interestingly when combined with weight loss, no additional effect was noted! [14]

Does low carb (Atkins diet) benefits cholesterol levels?

Recent meta-analysis demonstrated that Atkins diet increased both LDL and HDL cholesterol. Total cholesterol and triglycerides were reduced as well. it remains to be seen how this affect risk of heart attack and stroke! [15] Traditional Chinese Herbal Medications (Please consult Traditional Chinese Medicine Physician before starting those meds) Jiangzhitongluo capsule, Salvia miltiorrhiza and Pueraria lobata capsule, and Zhibitai capsule have a potent lipid-lowing effect (similar to statins) but there is no clinical data to evaluate their effects on risk of death and heart disease.

How to lower triglycerides?

- Lose weight
- · Restrict carbs and alcohol intake
- Increase consumption of unsaturated fats (olive oil, peanut butter, nuts)
- Restrict intake of saturated fats
- Increase consumption of omega 3 fatty acids (fish, fish oil, flaxseed, walnuts) [16]

Exercise and Triglycerides

When compared with the elevated levels that occur following a meal, triglyceride levels decreased 72 percent after a combined short, low intensity exercise program of walking and light resistance training (30 min), 1 hour after meal. In contrast, brisk walking and resistance training prior to eating decreased triglyceride levels by only 25 percent. Of course, it is challenging to exercise after each meal but if you have high triglycerides consider short activity after largest meal of the day. [17]

HDL: The Good Cholesterol (sometimes...)

Levels of high-density lipoprotein (HDL) cholesterol are generally inversely associated with the risk for the development of atherosclerosis. The mechanism by which HDL imparts protection from the initiation and progression of occlusive vascular disease is complex and multifactorial. The major anti-atherosclerotic effect of HDL is felt to be reverse cholesterol transport. HDL has been demonstrated to scavenge cholesterol from the peripheral vasculature with transport to the liver, where is it excreted in the biliary system.

It is very complicated....

In a very large study of 631,762 individuals there were 17,952 deaths during a mean follow-up of 4.9 ± 0.4 years. Individuals with lower HDL levels were independently associated with higher risk of cardiovascular, cancer, and other mortality compared with normal HDL values. In addition, individuals with higher HDL levels (>70 mg/dl in men, >90 mg/dl in women) had increased risk of non-cardiovascular mortality. [18]

In Dallas Heart Study of 2924 adults investigators observed that systemic inflammation changes HDL particle making it dysfunctional. Myeloperoxidase (MPO), a product of systemic inflammation, promotes oxidation of lipoproteins (both LDL and HDL) Highest versus lowest MPO/HDL particle ratio was associated with 74 percent increase in a combined endpoint of first non-fatal myocardial infarction, non-fatal stroke, coronary revascularization, or CVD death. [19]

HDL particles come in 3 sizes, large and small. Only large and medium particles were associated with removal of cholesterol from the plaque. Small particles did the opposite and promoted plaque buildup! [20]

Small HDL particle size appears to represent another feature of the high triglyceride-low HDL cholesterol dyslipidemia found in viscerally obese (big belly) subjects characterized by hyperinsulinemia (elevated insulin levels) as seen in patient with pre-diabetes and diabetes. [21]

Acute (such as flu) or chronic systemic inflammation and the metabolic syndrome appear to render HDL proinflammatory (promoting inflammation). In contrast, statins render HDL more anti-inflammatory. [22]

In the setting of potent statin therapy, HDL particle number is a better marker of residual risk than chemically measured HDL levels. [23]

Attempts to increase HDL cholesterol levels (with medications called CTEP inhibitors) yielded mixed results with 2 studies negative and 1 positive (ie. preventing heart attacks).

Smoking lowers HDL levels and changes its function, quitting increased HDL. [24]

So, what to do about HDL?

HDL seems to be a marker of your general health and socioeconomic status. Do not focus on a number but on lifestyle!

References:

- 1. Nissen, S.E. and C. From Cleveland Clinic, Ohio., *Statin Denial: An Internet-Driven Cult With Deadly Consequences*. Annals of Internal Medicine, 2017. **167**(4): p. 281-282.
- 2. Zhang, H., et al., Continued Statin Prescriptions After Adverse Reactions and Patient Outcomes: A Cohort Study. Annals of Internal Medicine, 2017. **167**(4): p. 221-227.
- 3. Prof Rory Collins, C.R., FRCP (Glasg.), Jonathan Emberson, PhD, et al., *Interpretation of the evidence for the efficacy and safety of statin therapy The Lancet.* The Lancet, 2016. **388**(10059): p. 2532-2561.
- 4. Hawkes, N., *Patients told about muscle pain are more likely to report it, statin study finds.* BMJ, 2017. **357**(j2144).
- 5. Martin, S.S., et al., *Dyslipidemia, coronary artery calcium, and incident atherosclerotic cardiovascular disease: implications for statin therapy from the multi-ethnic study of atherosclerosis.* Circulation, 2014. **129**(1): p. 77-86.
- 6. Miedema, M.D., et al., *Use of coronary artery calcium testing to guide aspirin utilization for primary prevention: estimates from the multi-ethnic study of atherosclerosis.* Circ Cardiovasc Qual Outcomes, 2014. **7**(3): p. 453-60.
- 7. Halverstadt, A., et al., Endurance exercise training raises high-density lipoprotein cholesterol and lowers small low-density lipoprotein and very low-density lipoprotein independent of body fat phenotypes in older men and women. Metabolism, 2007. **56**(4): p. 444-50.
- 8. Rocco, D.D., et al., *Aerobic exercise improves reverse cholesterol transport in cholesteryl ester transfer protein transgenic mice.* Lipids, 2011. **46**(7): p. 617-25.
- 9. Varady, K.A., A.H. Houweling, and P.J. Jones, *Effect of plant sterols and exercise training on cholesterol absorption and synthesis in previously sedentary hypercholesterolemic subjects*. Transl Res, 2007. **149**(1): p. 22-30.
- 10. Ornish, D., et al., *Intensive Lifestyle Changes for Reversal of Coronary Heart Disease*. JAMA, 1998. **280**(23): p. 2001-2007.
- 11. Jenkins, D.J.A., et al., Effect of a Dietary Portfolio of Cholesterol-Lowering Foods Given at 2 Levels of Intensity of Dietary Advice on Serum Lipids in Hyperlipidemia: A Randomized Controlled Trial. JAMA, 2011. **306**(8): p. 831-839.
- 12. Macchi, C., et al., Efficacy and safety of a nutraceutical with probiotic and red yeast rice extract in patients with moderate hypercholesterolemia: A randomized, double-blind, placebo-controlled study. Atherosclerosis, 2017. **263**: p. e109.
- 13. Pal, S., V. Ellis, and S. Dhaliwal, *Effects of whey protein isolate on body composition, lipids, insulin and glucose in overweight and obese individuals.* Br J Nutr, 2010. **104**(5): p. 716-23.
- 14. Richard, C., et al., Effect of the Mediterranean diet with and without weight loss on surrogate markers of cholesterol homeostasis in men with the metabolic syndrome. Br J Nutr, 2012. **107**(5): p. 705-11.
- 15. Mansoor, N., et al., *Effects of low-carbohydrate diets v. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomised controlled trials.* Br J Nutr, 2016. **115**(3): p. 466-79.
- 16. Miller, M., et al., *Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association*. Circulation, 2011. **123**(20): p. 2292-333.

- 17. Aoi, W., et al., Combined light exercise after meal intake suppresses postprandial serum triglyceride. Med Sci Sports Exerc, 2013. **45**(2): p. 245-52.
- 18. Ko, D.T., et al., *High-Density Lipoprotein Cholesterol and Cause-Specific Mortality in Individuals Without Previous Cardiovascular Conditions.* JACC, 2016. **68**(19).
- 19. Khine, H.W., et al., Association of the serum myeloperoxidase/high-density lipoprotein particle ratio and incident cardiovascular events in a multi-ethnic population: Observations from the Dallas Heart Study. Atherosclerosis, 2017. **263**: p. 156-162.
- 20. Mutharasan, R.K., et al., *HDL efflux capacity, HDL particle size, and high-risk carotid atherosclerosis in a cohort of asymptomatic older adults: the Chicago Healthy Aging Study.* J Lipid Res, 2017. **58**(3): p. 600-606.
- 21. Pascot, A., et al., Reduced HDL particle size as an additional feature of the atherogenic dyslipidemia of abdominal obesity. Journal of Lipid Research, 2001. **42**: p. 2007-2014.
- 22. Ansell, B.J., et al., *High-density lipoprotein function recent advances*. J Am Coll Cardiol, 2005. **46**(10): p. 1792-8.
- 23. Mora, S., R.J. Glynn, and P.M. Ridker, *High-density lipoprotein cholesterol, size, particle number, and residual vascular risk after potent statin therapy.* Circulation, 2013. **128**(11): p. 1189-97.
- 24. Forey, B.A., et al., *The effect of quitting smoking on HDL-cholesterol a review based on within-subject changes*, in *Biomark Res.* 2013, BioMed Central. p. 26.

High blood pressure is a common disease that puts you at risk for stroke, heart attack, kidney disease, heart failure and other serious problems. Most people with high blood pressure have no symptoms.

When your doctor or nurse tells you your blood pressure, he or she will say 2 numbers, e.g. "160 over 100." The first number (systolic blood pressure) is the pressure inside your arteries when



your heart contracts (systole). The second number (diastolic blood pressure) measures the pressure in your arteries when your heart is relaxed (diastole).

Recommended blood pressure treatment goals (new AHA guidelines as of 11/13/2017*):

* Please note: the American Academy of Family Physicians refused to endorse the new guidelines below and recommend keeping 140/90 threshold to start treatment (and a threshold of 150/90 for those over 60 years of age). Go figure!

Classification of elevated blood pressure:

	Systolic	Diastolic
Normal	Less than 120 mmHg	Less than 80 mmHg
Elevated	120-129 mmHg	Less than 80 mmHg
Stage 1 - Hypertension	130-139 mmHg	80-89 mmHg
Stage 2 - Hypertension	140 mmHg or higher	90 mmHg or higher

Treatment: medication and lifestyle changes:

Medication your doctor prescribes depends on your blood pressure measurements and other medical problems. Recent research suggests that rather than using maximum dose of a single blood pressure medication, combining several medications at lowest dose is more effective and associated with less side effects.

Certain drugs may lead to high blood pressure!

- Nonsteroidal anti-inflammatory drugs (NSAIDS): for example Ibuprofen (Advil, Motrin), Naproxen (Alieve), Diclofenac (Voltaren)
- Cough and allergy medications: pseudoephedrine (Sudafed)
- Birth control pills
- Supplements: Ephedra, Ginseng, natural licorice

- Steroids: for example, prednisone
- Antidepressants: Venlafaxine (Effexor)
- Amphetamines: for example meds used for treatment of ADD such as Adderall, Focalin, Ritalin

For more comprehensive list of medication causing high BP go to: (https://www.uspharmacist.com/article/drug-induced-hypertension).

Always notify your doctor and pharmacist of all the medications (including over the counter) as well as supplements.

Lifestyle changes:

Frequently changing your lifestyle will either result in reduction of medications you take or even elimination of blood pressure pills!

DASH diet: Simply the best for patients with high blood pressure!

DASH diet is definitely best approach to prevent hypertension and lower your BP. It is high in fiber, potassium, calcium and low in simple carbs, saturated fats and sodium. DASH diet with a low sodium level led to a mean systolic blood pressure that was 7.1 mm Hg lower in participants without hypertension, and 11.5 mm Hg lower in participants with hypertension. [4] It is much more effective than restricting sodium alone and it is still effective even if slat consumption is higher than recommended. For a 2,000-calorie diet, you should aim each day for six to eight servings of grains; four to five each of veggies and fruit; two to three of dairy; six or fewer of lean meat, poultry and fish, with one serving being equivalent to an ounce; four to five (a week) of nuts, seeds and legumes; two to three of fats and oils; and five or fewer (a week) of sweets. DASH suggests capping sodium at 2,300 milligrams a day and eventually working to stay at about 1,500 milligrams. Aggressive benefits of sodium restriction in high blood pressure haven recently questioned in a very large study. (See Chapter 2, Ref # 41)

More on DASH diet & recipes: (https://www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf)

Potassium intake:

Increasing consumption to 4.7 g per day (Recommended intake) lowers systolic blood pressure up to 3.2 mm Hg. [2]

Potassium rich foods include fruits (such as tomatoes, oranges, apricots, and bananas), vegetables, whole grains, dairy products and coffee.

Weight loss:

Maintaining a healthy weight provides many health benefits. If you are overweight, losing as little as five to 10 pounds may help lower your blood pressure! (Often equivalent to one BP medication)

Exercise: for at least 30 minutes a day on most days of the week! (Cardio and weights)



Lifting and High Blood pressure:

You shouldn't lift weights if your blood pressure is uncontrolled: higher than 180/110 millimeters of mercury (mm Hg). If your blood pressure is higher than 160/100 mm Hg, check with your doctor before starting a weightlifting program to discuss any precautions. Weightlifting can cause a temporary increase in blood pressure. This increase can be quite dramatic, as the weight

increases! Individuals (typically bodybuilders!) can experience very significant spike in blood pressure while weightlifting. The greatest peak pressures occurred during the double-leg press where the mean value for the group was 320/250 mmHg, with pressures in one subject exceeding 480/350 mmHg! [3]

Short spikes in BP during moderate lifting are not a problem, moderate lifting in long term lowers BP!



Specific foods effectively lowering effectively lowering blood pressure: (make it part of DASH or Mediterranean Diet plan)

Beet juice: It is high in natural nitrates. Saliva converts of nitrate to nitrite (facilitated by bacterial anaerobes situated on the surface of the tongue) which relaxes blood vessels and drops systolic BP by 10 mm Hg! [5]

Effective amount is between 250 and 500 ml per day.

Where to get it?

- Make your own: using preferably masticating juicer (Wholefoods sells loose beets)
- Buy premade (expensive!)
- Use beet powder (available on Amazon).
- Ground flax seed: Most potent effect: 15 mm H systolic BP drop in patients with hypertension!!

Just 1 ounce a day.
Cost? \$ 5 per month.
Side effects? Just few more trips to the toilet and little more gas...





Flaxseed contains ω -3 fatty acids, lignans (see explanation below), and fiber that together may provide benefits to patients with cardiovascular disease. In a prospective, double-blinded, placebo-controlled, randomized trial of 110 patients ingesting a variety of foods that contained 30 g of milled flaxseed or placebo each day over 6 months. Plasma levels of the ω -3 fatty acid α -linolenic acid and enterolignans increased 2- to 50-fold in the flaxseed-fed group but did not increase significantly in the placebo group. Patient body weights were not significantly different between the 2 groups at any time. SBP was \approx 10 mm Hg lower, and DBP was \approx 7 mm Hg lower in the flaxseed group compared with placebo after 6 months. Patients who entered the trial with a SBP \geq 140 mm Hg at baseline obtained a significant reduction of 15 mm Hg in SBP and 7 mm Hg in DBP from flaxseed ingestion. The antihypertensive effect was achieved selectively in hypertensive patients.

What are plant lignans?

Lignans are compounds that form the building blocks of plant cell walls. They contain phytoestrogens that help regulate the body's estrogen production. When we eat plant foods the lignan compounds are converted in our intestines by good bacteria to produce a form that the body can assimilate. Enterolactone the primary lignan metabolite (converted by bacteria in the gut)) that circulates in our blood produces weak estrogenic (sex hormone) activity. Multiple reports have revealed that high levels of enterolactone in blood reduces risk of breast, prostate and colon cancers, as well as cardiovascular disease. Studies have also shown that high levels of lignans can support healthy weight and glucose metabolism, reducing the risk of insulin sensitivity, metabolic syndrome and diabetes. Lignan precursors are found in a wide variety of foods, including flaxseeds, sesame seeds, legumes, whole grains, fruit, and vegetables. [6]

Hibiscus tea

At 6 wk hibiscus tea lowered systolic BP (SBP) compared with placebo by over 7 mm Hg. This was accomplished with 3 servings of 240 ml a day. No side effects of this therapy were reported. [7]

Other food which effective in lowering BP are: dark chocolate, berries, oranges, olive oil, pistachios, pomegranates, dairy, fatty fish, whole grain, garlic, and were discussed in the "You are what you eat"



chapter. Please note than those foods are part of the DASH and Mediterranean diets!

Traditional Chinese Herbal Medications:

Tiankuijiangya, Zhongfujiangya, Qiqilian, Jiangya and Jiangyabao have been shown to be very effective and safe in lowering BP, with effect similar to prescription antihypertensives.

Acupuncture:

160 outpatients with uncomplicated, mild to moderate hypertension were randomized to six weeks of acupuncture performed by Chinese medicine practitioners (needles where inserted in prespecified points known in Chinese medicine to lower BP) or to a sham procedure (needles were inserted in different areas of the body). Patients underwent 22 sessions, each 30 minutes in length. By the end of the six weeks, 24-hour ambulatory systolic and diastolic blood pressures were significantly reduced from baseline in the acupuncture-treated patients (5.4 mm Hg and 3.0 mm Hg, respectively), and this change was also significantly different from values in the shamtreated patients, in whom no meaningful changes were seen. The effect was no longer observed after 3 or 6 months. It seems for acupuncture to be effective it has to be continued 2-3 x a week, which is a major time and financial commitment. [8]

White Coat Hypertension:

Stress is a major contributor to high blood pressure (by triggering fight and flight reaction). Some patients have high blood pressure just in doctor's office; "white coat hypertension" It is associated with over 2x increase in risk in cardiovascular event (death, stroke, heart attack) but only in those older than 60 years with 3 or more risk factors (such as smoking, diabetes, high cholesterol, previous heart issues or stroke) It had no effect on younger individuals as well as older and healthier ones. [9]

Masked hypertension: normal BP in doctor's office does not mean normal BP at home!

Masked hypertension is defined as a normal blood pressure (BP) in the clinic or office (<140/90 mmHg), but an elevated BP out of the clinic (ambulatory daytime BP or home BP>135/85 mmHg. There is strong evidence that masked hypertension patients have increased risk of target organ damage, cardiovascular, and renal morbidity with an overall cardiovascular risk approaching that of sustained hypertensive!

Which is the population of patients likely to have masked hypertension?

- Elderly (typically male) patients.
- Office measurement of BP in an elderly hypertensive patient soon after a large meal may produce postprandial reduction of BP.
- Mental stress at work or at home may raise BP to hypertensive levels except at the time of doctor office measurements. (For patients who are looking forward to seeing their doctor to get a break from stress at home!)
- Smokers and patients who consume excessive alcohol are prone to masked hypertension. [10]

Stress, Anger and Blood Pressure:

Negative emotions significantly contribute to high blood pressure!

The following approaches have been shown to be very effective in lowering blood pressure especially if you deal with stressful situation:

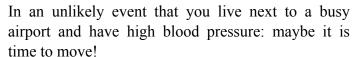
- Laughter
- Yoga
- Meditation
- Tai Chi
- Biofeedback: Resperate is an FDA approved device which lowers BP on average 14/9 mm Hg, with 10 percent of patients (likely the most stressed) achieving reduction of 36/20 mm Hg! For more information go to: (http://www.resperate.com/)

Side effects? *Happiness!*



Monitoring BP at home: make sure you have right equipment:

Home BP monitoring may not be as accurate as we hoped. The proportion of devices with systolic or diastolic BP differences from auscultation of ≥5, 10, and 15 mm Hg was 69 percent, 29 percent, and 7 percent, respectively. Increasing arm circumference was a statistically significant predictor of higher systolic and diastolic blood pressure. Bring your blood pressure cuff the office and compare it with doctor's office BP! [11]







Investigators studied 420 people living near Athens International Airport. The researchers "found that for each 10-decibel increase in noise at night, the risk of developing hypertension more than doubled! [12]

Spending time in the sauna prevents hypertension.

Spending time in sauna not only did reduce blood pressure but prevented from even developing this problem. A study from (not surprisingly) Finland of over 1600 men observed over 24 years concluded the more frequently you visit sauna the lower lifetime risk of getting high blood pressure:



2-3x a week reduced it by 17 percent, 4-7 sessions per week by 46 percent compared to those who attended only once a week! [13]



With a broken body clock, even a low salt diet can raise resting blood pressure!

In the face of a disrupted circadian rhythm, a low-salt diet and a hormone known to constrict blood vessels have the same unhealthy result: elevated resting blood pressure and vascular disease. Sleep or rest time is when our 24-7 organs should get at least a bit of a break. It also appears to be a time circadian dysfunction can be silent and dangerous. When resting blood pressures don't drop as they should, it's called nondipping.

Animal studies demonstrated that low sodium diet (as expected) lowered BP in mouse model. But when low-salt diet was fed to a mouse that had a circadian dysfunction, (basically a sleep disorder which in humans would correspond to any condition which disrupt sleep including snoring wife), low sodium actually causes this nondipping blood pressure and vascular disease.

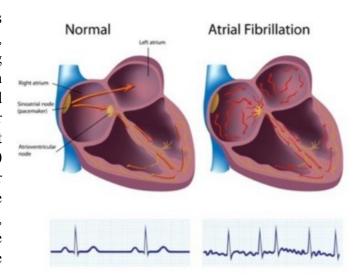
Low salt diet is known in humans and animals to stimulate the renin-angiotensin-aldosterone system, which helps regulate blood pressure by prompting blood vessel constriction and holding onto fluids in the body.

The important message form this study is that a 24-hour blood pressure check (your doctor can prescribe a 24 hour BP monitor) may reveal previously hidden nondipping blood pressure (situation where your BP is well controlled during the day but does not drop as it should at night) [14]

References:

- 1. Cutler, J.A., D. Follmann, and P.S. Allender, *Randomized trials of sodium reduction: an overview.* Am J Clin Nutr, 1997. **65**(2 Suppl): p. 643s-651s.
- 2. Press, N.A., Front Matter | Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate | The National Academies Press. 2005, Food and Nutrition Board Instit of Medicine.
- 3. MacDougall, J.D., et al., *Arterial blood pressure response to heavy resistance exercise*. J Appl Physiol (1985), 1985. **58**(3): p. 785-90.
- 4. Sacks, F.M., et al., *Effects on Blood Pressure of Reduced Dietary Sodium and the Dietary Approaches to Stop Hypertension (DASH) Diet.* The New England Journal of Medicine, 2001. **344**: p. 3-10.
- 5. Webb, A.J., et al., *Acute blood pressure lowering, vasoprotective, and antiplatelet properties of dietary nitrate via bioconversion to nitrite.* Hypertension, 2008. **51**(3): p. 784-90.
- 6. Rodriguez-Leyva, D., et al., *Potent Antihypertensive Action of Dietary Flaxseed in Hypertensive Patients*. Hypertension, 2013. **10**(14).
- 7. McKay, D.L., et al., *Hibiscus sabdariffa L. tea (tisane) lowers blood pressure in prehypertensive and mildly hypertensive adults.* J Nutr, 2010. **140**(2): p. 298-303.
- 8. Flachskampf, F.A., et al., *Randomized Trial of Acupuncture to Lower Blood Pressure*. Circulation, 2007. **115**: p. 3121-3129.
- 9. Franklin, S.S., et al., *The Cardiovascular Risk of White-Coat Hypertension*. JACC, 2016. **68**(19).
- 10. Franklin, S.S., et al., *Masked Hypertension*. Hypertension, 2015. **65**: p. 16-20.
- 11. Ringrose, J.S., et al., An Assessment of the Accuracy of Home Blood Pressure Monitors When Used in Device Owners. American Journal of Hypertension, 2017. **30**(7): p. 683-689.
- 12. Dimakopoulou, K., et al., *Is aircraft noise exposure associated with cardiovascular disease and hypertension? Results from a cohort study in Athens, Greece.* Occupational and Environmental Medicine, 2016.
- 13. Zaccardi, F., et al., Sauna Bathing and Incident Hypertension: A Prospective Cohort Study. Am J Hypertens, 2017.
- 14. Pati, P., et al., Low-Salt Diet and Circadian Dysfunction Synergize to Induce Angiotensin II-Dependent Hypertension in Mice. Hypertension, 2016. **67**(3): p. 661-8.

Atrial fibrillation (AF) initially occurs occasionally (known as paroxysmal AF), then increases in frequency requiring electrical shocks and medications to return and stay in rhythm (persistent AF) and eventually stays all the time and the doctor is no longer able to restore normal heart beat (permanent or chronic AF) Only 10 percent of all AF, have no clear etiology or trigger. Early in the disease AF can be prevented, as AF becomes more frequent, left atrium (the upper chamber of the heart) starts stretching promoting more atrial fibrillation: "AF begets AF".



Your cardiologist may recommend atrial fibrillation ablation procedure when the problem becomes more frequent and bothersome. AF ablation is not a cure! It is very effective but only if you eliminate what triggered it in first place!

AF is the most common cardiac arrhythmia, significantly influences health and health care. In the United States alone, 2.7 million to 6.7 million people have AF, one-third of the total AF population is asymptomatic. AF is associated with an increased risk for major health issues with 5-3 and 2-fold increased risk for stroke, heart failure, and dementia, respectively, and 40 to 90 percent increased risk for death. In the US AF costs Medicare 16 billion dollars a year!

Atrial Fibrillation Triggers:

Alcohol consumption

Drinking alcohol is a popular habit, with >50 percent of American adults are regular drinkers and an additional 13 percent reported to be infrequent drinkers. Even light to moderate alcohol consumption may increase the risk for AF: Just 1.5 drinks a day increased AF risk by 25 percent to 46 percent. Each additional drink per day is associated with an estimated 8 percent increase in relative risk for AF. The relationship between alcohol consumption and risk for AF appeared to

be linear, and there was no drink threshold below which alcohol consumption was safe! Translation: the more you drink the more AF.



Physical activity

Moderate physical activity and general physical fitness is associated with reduction of risk for atrial fibrillation. Very strenuous exercise, > 5 hours per week was associated with 10x increase in atrial fibrillation but only in men. Avoiding a sedentary lifestyle should be considered an important way to avoid the hazards of AF.

Negative emotions

Stress has been shown to be responsible for 54 percent of AF episodes. Panic disorder was also reported to be associated with a 73 percent higher risk for AF development during 7 years of follow-up. Negative emotions (anger, stress, impatience, anxiety) were associated with 3 to 6 fold higher risk for AF occurrence among patients with paroxysmal AF, whereas happiness had a protective effect reducing risk of atrial fibrillation by 88 percent! In summary, data indicate a strong link between negative emotions and an increased risk for AF. These studies offer new clues for interventions that could reduce the risk for AF.

Smoking

The Rotterdam study reported a 51 percent higher risk for AF development among current and former smoker. Even exposure to secondhand smoke during gestational development and childhood was associated with higher AF risk later in life! Once you quit, risk goes down.

Obesity

A meta-analysis of cohort studies revealed that in the general population, obesity increased the risk for AF by 49 percent. In all studies, body mass index (BMI) had a linear association with AF risk: with each unit increase in BMI, AF risk increased by 4 percent to 8 percent. The effect of obesity on the risk for AF starts very early; even birth weight was significantly associated with AF risk later in life! Weight gain from age 20 to midlife is also a risk factor for AF: with 16 percent to 35 percent had >35 percent weight gain, AF risk increased by 34 percent and 61 percent, respectively. 18 percent of cases of AF in US could be prevented by achieving an optimal body weight for patients who had a 10 percent or greater weight loss, 3 percent to 9 percent weight loss, and those with <3 percent weight loss or weight gain, the probability of freedom from AF in the absence of antiarrhythmic drug or ablation procedure was 45.5 percent, 22.2 percent, and 13.4 percent. Weight loss through bariatric surgery may reduce the risk for incident AF by approximately one-third among persons being treated for severe obesity.

High Blood Pressure

For every 10 mm Hg increase in systolic blood pressure, the risk for AF increases by 11 percent. High blood pressure is the most important contributor to the burden of AF. Optimal blood pressure control significantly reduces AF occurrence in patients with hypertension. In a prospective observational study, poor blood pressure control was associated with a 7-fold higher risk for developing new-onset AF during 2 years of follow-up.

Diabetes

Diabetes to be associated with a 34 percent increased risk for AF. In a population-based case-control study, the risk for developing AF was 3 percent higher for each additional year of diabetes duration. With each 1 percent increase in glycated hemoglobin (hemoglobin A1C), the risk for AF increased by 13 percent and 5 percent in patients with and without diabetes, respectively.

Obstructive Sleep apnea

Obstructive sleep apnea increased risk of AF over 2 times! Nocturnal oxygen desaturation (drop in oxygen level at night), a consequence of OSA, was found to be an independent risk factor for incident AF in subjects <65 years of age increasing risk of AF 3.3 times. The odds of AF's occurring within the 90-second hazard period following a respiratory disturbance (when you quit breathing and oxygen levels plummet) were 17.9-fold greater than the odds of AF's occurring during normal breathing. Treatment with continuous positive airway pressure (CPAP) among patients with OSA and paroxysmal AF may reduce AF recurrence. 12 months after cardioversion (electric shock to restore regular heart beat), AF recurrence rates were 82 percent, 42 percent, and 53 percent in untreated patients, CPAP-treated patients, and those without OSA, respectively. Presence of sleep apnea significantly affects outcomes of AF ablation therapy among patients with AF with OSA: 36.7 percent vs. 66.7 in patients with normal sleep. Using CPAP dramatically increased success rate to 72 percent!

Other cardiovascular disease

Heart failure and AF are also closely related: left atrium is fairly thin, excessive amount of fluid as seen in heart failure stretches it, disrupting normal flow of electricity. About one-third of patients with heart failure will develop AF; conversely, one-third of patients with AF will develop heart failure. Heart failure is associated with a 4.5-fold increased risk for AF in men and a 5.9-fold increased risk in women. The risk for AF is also high in heart failure with preserved ejection fraction (known as diastolic heart failure in which the heart pumping function is preserved but is too stiff to relax). A community-based study reported that AF occurred in 32 percent of patients who had heart failure with preserved ejection fraction over a median follow-up period of 3.7 years.

For more details, we recommend our source article, which we used to write this chapter:

Is Atrial Fibrillation a Preventable Disease? Journal of American College of Cardiology, Vol 69, No 15, 2017.

Diet

Contrary to popular beliefs coffee and chocolate consumption not only did not cause atrial fibrillation but reduced its risk! This statement does not apply to caffeinated soft drinks however. Fish consumption has been shown to reduce risk of atrial fibrillation. (Of course, not fried fish)

If you were diagnosed with atrial fibrillation, quick intervention could prevent it from becoming a chronic problem!

- 1. Quit drinking, completely!
- 2. Start moderate exercise routine (but avoid very strenuous activity > 5 hours per week if you are male!).
- 3. If you are obese or overweight any amount of weight loss will help! For best results aim at 10 percent body weight loss.
- 4. Quit smoking.
- 5. Ask your doctor to consider sleep study to see if you may have sleep apnea.
- 6. Make sure that blood pressure and blood sugar is well controlled.
- 7. Relax, practicing yoga has been shown to prevent 50 percent of atrial fibrillation!
- 8. Eat fish frequently and dark chocolate daily.

Success of treatment of AF (medications, ablation procedure) strictly depends on your commitment to life style change!

What is the CHA2DS2vasc score?

It is a simple way for your doctor to calculate the risk of a stroke if you do not take blood thinners:

Factors	Points
C: congestive heart failure	1
H: hypertension	1
A: age	
> 65	1
> 75	2
D: diabetes	1
S: sex (for females)	1
S: stroke	2

Recent data suggest that benefit outweighs risk of blood thinners when the score is 1 or higher.

Anticoagulation for atrial fibrillation

Many patients are reluctant to start blood thinners, which puts them not only at risk of stroke but also dementia. Even delaying blood thinners by just 1 month, increased risk of dementia 2.4 times![1]

References:

1. Du, X., J. Dong, and C. Ma, *Is Atrial Fibrillation a Preventable Disease?* J Am Coll Cardiol, 2017. **69**(15): p. 1968-1982.

Depression in patients with coronary artery disease (CAD) is the strongest predictor of death!

Patients (N = 24 137) who had angiographically determined CAD (stenosis \geq 70%) were studied. A total of 3646 (15%) had a depression diagnosis during follow-up. Death (mean follow-up: 9.7 \pm 6.1 years) occurred in 40 percent of patients (depression: 50% vs. no depression: 38%). Depression which occurred after CAD was the



strongest predictor of death. A depression diagnosis at any time following CAD diagnosis was associated with a two-fold higher risk of death.[1]

- Analysis of multiple clinical trials demonstrated that in mild to moderate depression medications known as SSRI (for example Paxil, Prozac) are not different is its efficacy than placebo.
- There are multiple medications, which may trigger depression. It typically starts within 30 days after the new medication was added. For a complete list of those medications go to: (http://www.rxeconsult.com/healthcare-articles/Review-of-Medications-That-Cause-Depression-749/)

Food and Depression

Can food affect our mood? Yes!

- A traditional whole-food diet, consisting of vegetables, fruits, seafood, whole grains, lean meat, nuts, and legumes, with avoidance of processed foods, is more likely to provide the nutrients that afford resiliency against mental disorders.
- The mechanisms by which nutrition might affect mental health are obvious: the human brain operates at a very high metabolic rate, and uses a substantial proportion of total energy and nutrient intake.
- Many epidemiological studies have shown associations between healthy dietary patterns and a reduced prevalence of, and risk for, depression and suicide.
- Recent research demonstrated a connection between unhealthy dietary patterns and poorer mental health in children and adolescents.[2]
- Results from the large European PREDIMED study showed a reduced risk for incident depression for individuals randomly assigned to a Mediterranean diet with nuts, and this protective effect was particularly evident in those with type 2 diabetes.

- Similarly, results of an indicated prevention trial showed that dietary counseling was as effective as psychotherapy at prevention of depression in older adults.
- Recent data suggest that select nutrient-based supplements might support neurochemical activities that are beneficial in the management of mental disorders.
- Examples of these nutrient-based supplements include omega-3 fatty acids, S-adenosyl methionine (SAMe), N-acetyl cysteine (NAC), zinc, B vitamins (including folic acid), and vitamin D.
- Various clinical investigations support the potential usefulness of omega-3 fatty for many mental disorders including, bipolar depression, post-traumatic stress disorder, and major depression, and they are indicated in the prevention of psychosis.

How to change your diet to combat depression

1. Reduce sugar and processed foods

Sugar, sugary foods, or even food that is converted quickly into sugar, such as many breakfast cereals, cause your blood sugar to rapidly rise. (High glycemic index) however two to three hour's later blood sugar levels starts to fall.

At this point, you may not only feel hungry, you can feel "h-angry" as well - hungry and angry.



Low and falling blood sugar levels can cause a rise in your body's stress hormones, cortisol and adrenaline and this has a negative impact on your mood.

2. Increase your intake of Omega-3 fats

This is an essential nutrient for brain function and may protect against anxiety and other psychiatric disorders.

Foods high in Omega-3 fats include fatty fish (salmon, mackerel, anchovies), grass-fed meat, seeds and leafy vegetables.



3. Eat more tryptophan-containing foods such as pork, turkey, chicken, pumpkin seeds and walnuts.

Tryptophan is an amino acid the body converts into serotonin, your feel-good neurotransmitter.





Eaten with a healthy carbohydrate source, such as sweet potatoes, helps to transport more tryptophan into your blood.

4. Feed your gut microbes our "Second Brain" Healthy population of gut bugs can have a significant influence on our mood via the gut-brain axis. (see Chapter 6 - The Human Microbiome)



The prebiotic fiber contained in vegetables help your gut bugs to proliferate, so the best way to maintain a healthy population is to increase your intake of vegetables (Best options are leeks, onions, garlic, artichokes and cruciferous vegetables like broccoli and cauliflower), as well as fermented foods (probiotics) such as sauerkraut. [3]

Laugh!

• Try to remove yourself from sources of negativity being a coworker, family member or negative news. Did you ever feel happy watching Fox News for an hour? When we laugh, our body produces nitrous oxide, which not only lowers blood pressure and improves blood flow through the heart muscle but also has antidepressant properties.



Sleep

Sleep deprivation and poor quality of sleep may lead to depression and worsen existing symptoms. Depression in turn affects negatively sleep quality. Practice sleep hygiene! (cbtforinsomnia.com)

How Honesty Could Make You Happier

Yes. Everybody lies...

Research from the University of Notre Dame has shown that when people consciously stopped telling lies, including white lies (see below for explanation), for 10 weeks, they had fewer physical ailments (like headaches) and fewer mental health complaints (like symptoms of depression and stress) than a control group that did not focus on honesty. In weeks when participants told fewer lies, they reported that their close personal relationships had improved and that their social interactions overall had gone more





smoothly that week, the study revealed. The **definition** of a **white** lie is a harmless fib or a small untruth, often done to spare someone's feelings or for some other diplomatic reason. An example of a **white** lie is when you tell your mother in law that her pie is good even when it tastes terrible. [4]

Pray and meditate

• Before falling asleep write down 5 things you are thankful for! Focus on present moment: this is your fortress; no one can hurt you when you are there. Start with simple breathing exercise Join a meditation group or yoga class with focus on meditation. Learn contemplative prayer. Spend more time with the nature. Turn off your cell phone for 1 hour. Try to be mindful in your

daily life for example while driving, eating,

washing dishes etc.

• Volunteer and practice random act of kindness: as the depressions worsen we tend to isolate ourselves from others and submerge in our own negative thoughts. The more you think of others, the happier you become.



Exercise

Any Intensity Level of Exercise Can Lift Your Mood!!!!!

Light levels of exercise (defined as activity not changing heart rate, example strolling through a mall) were found to lead to higher levels of psychological well-being and lower levels of depression, while moderate levels of exercise (with increased heart rate) were linked to not only



better psychological well-being, but lower levels of pain severity. [5]

It makes a difference if you walk in nature versus an urban area!

Scientists investigated effect a walk might have on a person's tendency to brood. Brooding, also known as morbid rumination, is a mental state in which we can't seem to stop replaying in our mind what is wrong with our life and ourselves. This is often a precursor to depression and is much more common among city dwellers compared with people living outside urban areas. Rumination also is strongly associated with increased activity in a portion of the brain known as the subgenual prefrontal cortex. Scientists randomly assigned



half of the study participants to walk (alone, no music) for 90 minutes through a leafy, quiet, park or next to a loud, hectic, multi-lane highway. Immediately after completing their walks, the participants underwent functional MRI of the brain not surprisingly; walking along the highway had not soothed participant's minds. Blood flow to their subgenual prefrontal cortex remained high and their broodiness scores were unchanged. But the participants who walked through a park showed improvements in their mental health (no longer "stuck" on negative aspects of their

life) and experienced significant decrease in blood in the subgenual prefrontal cortex. This strongly suggests that getting out into natural environment is an easy and almost immediate way to improve moods for city dwellers.[6]





Have more sex!

Yes, sex has antidepressant properties! For more details see reference section. As this book is rated PG 13, we decided not to go into the juicy details of this study.[7]

References:

- 1. May, H.T., et al., The Association of Depression at Any Time to the Risk of Death Following Coronary Artery Disease Diagnosis. Eur Heart J Qual Care Clin Outcomes, 2017.
- 2. O'Neil, A., et al., Relationship between diet and mental health in children and adolescents: a systematic review. Am J Public Health, 2014. 104(10): p. e31-42.
- 3. Chatterjee, B.-D.R., How food can improve your mental health BBC News. 2017.
- 4. Kelly, A.E., A Life without Lies: How living honestly can affect health, in American Psychological Association 120th Annual Convention. 2017: Washington, DC.
- 5. Panza, G.A., et al., Physical activity intensity and subjective well-being in healthy adults. http://dx.doi.org/10.1177/1359105317691589, 2017.
- 6. Bratman, G.N., et al., *Nature experience reduces rumination and subgenual prefrontal cortex activation*. 2015.
- 7. Gallup, G., R. Burch, and S. Platek, *Does Semen Have Antidepressant Properties?* Archives of Sexual Behavior, 2002. **31**(3): p. 289-293.



It is only when a mosquito lands on your testicles that you realize there is always a way to solve problems without using violence.

"Between stimulus and response there is a space. In that space is our power to choose response. In our response lies our growth and our freedom"

- Victor Frankl, author of "Man's Search for Meaning"

Dealing with Anger was written by Timothy Raine, Director of The Christ Hospital "Living with pain" meditation program

Anger, one of the Seven Deadly Sins, is also considered by some traditions to be the "most dangerous of the destructive emotions." A 6th century Indian sage says anger is: an evil incongruent with any other; an evil of which a single flash will shatter good works gathered in a thousand ages; a pain that torments those subject to it and prevents: tranquility of mind and familiarity with pleasure, sleep, and rest; the cause of hate that leads to attack by enemies and subordinates alike; and the cause of estrangement from friends, families, joy, happiness, and peace. Modern medical science has also demonstrated that anger can be an exacerbating factor in:

- Anxiety
- Asthma
- Cancer
- Chronic pain
- Depression
- Heart disease
- High blood pressure
- Irritable bowel syndrome
- Sleep problems
- Tension headaches

Therefore, it seems very important that we learn to deal with, or manage, anger. In order to learn to do so effectively, we must first understand what anger is and where it comes from. Thousands of years ago, our hunter-gatherer ancestors lived in very dangerous environments, where their lives were at risk of being taken suddenly and violently, where they might become food for predators. Over the millennia they evolved a defensive mechanism which modern psychology describes as "fight, flight, or freeze." If confronted with an existential threat, they would immediately react by either viciously attacking the person or animal who threatened, running as fast as possible to escape the threat, or remaining completely immobile, hoping the threat would pass. These reactions served to ensure the survival of the individual and the continuation of the species, allowing homo sapiens to become what we are now. Over thousands of years, and through repeated exposures to such circumstances, our brains have evolved to be hardwired for self-protection. In our lives today, we rarely (if ever) actually face such immediate threats to our lives; however, we still retain this kind of reactive capability. But instead of using them in the face of predators, we employ them to deal with different kinds of threats, such as: The boss

criticizes our work, someone points out our short-comings. We are admonished for behavior someone finds offensive, we believe we are being treated unfairly or disrespectfully ('dissed'), the car won't start, the computer crashes, the check-out line isn't moving fast enough, or any expectation or strong desire is frustrated or isn't met.

These are not life-threatening events, but we do perceive them as assaults on our ego, our sense of self, who we are, what we value. And we react to these perceived threats in exactly the same way, but perhaps with a bit lesser intensity. So our brain and body dump a load of stimulant and inflammatory chemicals into our blood system to enable us for combat. In these situations, however, we cannot lash out and hit the boss (fight); and we probably can't just leave the building (flight); and if we just stand there (freeze), we'll feel even more inadequate, making things even worse. If we were able to run, hit, etc., our bodies would naturally metabolize the stress chemicals, such as adrenaline, norepinephrine. But because we cannot do those things, we remain awash in them. We now know that it takes 60-90 minutes for our body to restore equilibrium without the physical exertion of *flight-or-fight*; and during that time, we often have another experience that triggers a similar reaction. This long-term imbalance and exposure to stress chemicals that seems to have the effects noted above. So, knowing that held-in anger is destructive for ourselves and outwardly expressed and is destructive for those around us, why is it so hard to stop dealing with anger in these ways? The answer is simple: we want to be angry, because the small mind of anger wants nothing more than to be right. There's a feeling of juiciness and power that accompanies the expression of anger, stemming from the body chemistry associated with it, and this feeling can be quite intoxicating. In fact, neuroscience tells us that "neurons that fire together wire together," which means that any repeated behavior, especially one with so much emotional charge, is likely to become an addiction! In other words, while venting might provide short-term relief, it actually is strengthening the neural pathways encouraging repeated outbursts.

What to do, then, about anger? The first step is to learn to recognize anger for what it is before the expression or explosion. You might think, "I always know when I'm angry." But most of us our first recognition only comes when we are already in the middle of the reaction. We can train this early warning system by becoming more aware of what is happening in the body in the moment it is happening. Anger is often accompanied by strong sensations: a feeling of heat, breath becoming shallower and faster, tightness in the chest, neck, and throat, and abdomen, and maybe even a clenching of fists or pounding of the heart. At the same time, we can learn to sense the increased agitation in the mind, along with a sharpening of focus on the object of our anger. Just this first step can begin the process of de-fusing anger.

Next, we investigate in as much detail as possible. What triggered this reaction? Without making up a whole long story about the events leading up to this, just list the facts in the order they occurred as dispassionately as possible, much like a detective: just the facts. What are/were all of the bodily sensations? How intensely did I feel them? What was my state of mind? What is/was the story I told myself about these happenings and what I took their meaning to be? Is the story actually true, or is there some other possible story?

If when similar events occur in the future, is there some other possible way I can respond? In the beginning, the recognition and investigation can only be done in retrospect, after the incident, and that's fine. Another way to train in this is through mediation practices. A practice known as the Body Scan aids us in becoming more acutely aware of bodily sensations, how they arise, and how they change or go away, how transient they are. Both the Body Scan and Sitting Meditations make us more familiar with the rhythms and sensations associated with the breath as it comes and goes. Walking Meditation and Hatha Yoga focus on slow movement and sensations of the breath so we become more aware of the body in motion. (Tai Chi and Qi Gong are also excellent.) As we become more adept at recognizing the events, external and internal that trigger anger in us, and more scrutinizing in our investigation, we can take another step in the heling process, and there are two meditation practices that are helpful. The first is called *metta* (it means loving-friendliness or kindness in ancient Pali). In this practice one begins by wishing for oneself such conditions as happiness, safety, health, peace, joy, ease of living. Then one extends those same wishes to family, friends, and loved ones. Next one extends those wishes to 'neutral' people, those we see but largely disregard in daily life. After that, we extend those wishes to the people in life whom we find to be difficult. And so we proceed until we can include everyone everywhere. All during this practice, we try to bear in mind that everyone wants the same things in life. Even more powerful is the forgiveness, which some people combine with the practice of metta. While it is recommended as a meditation practice, it can also be done in person, face-toface if you have the courage. We begin by bringing to mind someone we have hurt, physically or emotionally. In true contrition, we ask their forgiveness. We also extend forgiveness to anyone whom we have hurt. As in the *metta* practice, we start with those closest to us, and move outward, increasing the circle of inclusion. We end by extending the same forgiveness to ourselves. Throughout this practice, we try to bear in mind that, at any given time, everyone is doing the best they can with the tools they have in their circumstances. Over time, a consistent meditation practice will reduce emotional reactivity, bringing about a paradigm shift that mobilizes one's inner resources and opens the way to personal growth and development, fostering a sense of well-being and healing. One recognizes that self-worth is not tied to events, but arise from within, and that occurrences are just stuff that happens, mostly impersonally, and that they don't require any response at all.

Another ingredient in dealing with anger is patience. We can cultivate patience, along with equanimity (emotional balance) through a number of meditation practices. When we bring patience to a distressing situation that might evoke anger in us, we can just pause, take a few deep breaths (preferable what is called 'belly breathing'), and wait for our emotions to subside, as they inevitably will. In fact, learning to pause and take a few breaths in any situation will help you to see things more clearly and dispassionately, and will provide the opportunity to respond more creatively and constructively. Finally, learning the skills of clear and uncomplicated communication can help to avoid the kinds of personal conflicts that often give rise to reactive anger. An excellent resource is *Crucial Conversations* by Patterson, Grenny and McMillan. This book invokes mindfulness as a beginning for such conversations in the first step: Start With Heart.

Our communication styles and habits, like our anger reactions, have been learned over many years, and reinforced over and over again, perhaps thousands of times. It is wise to remember this, and understand that it will take the same kind of rehearsal and practice over time to bring about real change. Each time we pause, breathe, and open the window of opportunity, we weaken the habitual neural pathways and create or strengthen new ones, leading to a new way of seeing the stressors in life, and a better way of dealing with them. We will never be able to get rid of anger; it is a built-in self-preservation mechanism. But we can reduce our reactive tendencies by seeing and understanding them. All we have to do is practice.

Pets Benefit the Heart (But don't get a pet just for this reason!)

- A 2009 study looking at 4,435 participants found that owning cats as domestic pets decreased the relative risk (0.63) for death from a heart attack. [1]
- A 2013 study consisting of 240 married couples found that those who are pet owners have a significantly lower blood pressure (both systolic and diastolic) than non-pet owners. [2]
- Pet owners also had a lower total cholesterol level (201 vs 206mg/dL) and lower triglyceride levels (108 vs 125mg/dL) compared to non-pet owners. [3]
- Pet owners are 54 percent more likely to obtain the recommended physical activity recommendations compared to non-owners. [4]
- Non-pet owners have 2-fold higher odds of being obese compared to dog walkers/dog owners and non-dog walkers/dog owners had 60 percent higher odds. [5]
- A study with 369 participants with established CVD found that dog ownership was associated with decreased mortality. Those who did not own dogs had a 4.05 times the greater risk of mortality. [6]
- Dog owners on average walked 22 minutes more per day compared to people who didn't own a dog. In addition, they spend much less time sitting! It all ads up to cardiovascular health! [7]



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Pets and Your Heart

Owning a dog makes you live longer

Using national registries in Sweden to track the lives of over 3.4 million citizens who had no prior history of cardiovascular ailments back in 2001, the study followed the health status of each individual over many years. Sweden has mandatory dog ownership registration and national medical systems as such it was easy to link dog ownership to health outcomes.

Conclusion: having a dog reduces your overall mortality, with risk of death being almost 33 percent lower in dog owners who lived alone. That same group benefited from an 11 percent drop in risk of cardiovascular disease as well, when compared to their non-dog-owning peers. Those in multi-person households also had a lower risk of mortality if they owned a dog, and hunting breed dogs specifically helped to lower the risk of cardiovascular disease.

The reason for these trends is obvious: Dogs love to be outside and most of them require daily walks or play time to expend their energy. Dog owners are often motivated by their animals to get up off the couch and head outdoors, even if just for a short stroll, and those healthy behaviors resulted in decreased risk of death. Those who choose breeds for hunting would likely already be considered outdoorsy types, and regular exercise has long been associated with reduced risks of cardiovascular diseases. In addition, dogs unconditional love, lowers levels of stress!

If you find yourself being lazy but just can't work up the motivation to take a daily walk or jog, a dog might do the trick! [8]



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Pets and Your Heart

References:

- 1. Qureshi, A.I., et al., Cat ownership and the Risk of Fatal Cardiovascular Diseases. Results from the Second National Health and Nutrition Examination Study Mortality Follow-up Study, in J Vasc Interv Neurol. 2009. p. 132-5.
- 2. Allen, K., J. Blascovich, and W.B. Mendes, Cardiovascular reactivity and the presence of pets, friends, and spouses: the truth about cats and dogs. Psychosom Med, 2002. 64(5): p. 727-39.
- 3. Anderson, W.P., C.M. Reid, and G.L. Jennings, Pet ownership and risk factors for cardiovascular disease. Med J Aust, 1992. 157(5): p. 298-301.
- 4. Oka, K. and A. Shibata, Dog ownership and health-related physical activity among Japanese adults. J Phys Act Health, 2009. 6(4): p. 412-8.
- 5. Lentino, C., et al., Dog walking is associated with a favorable risk profile independent of moderate to high volume of physical activity. J Phys Act Health, 2012. 9(3): p. 414-20.
- 6. Friedmann, E. and S.A. Thomas, Pet ownership, social support, and one-year survival after acute myocardial infarction in the Cardiac Arrhythmia Suppression Trial (CAST). Am J Cardiol, 1995. 76(17): p. 1213-7.
- 7. Dall, P.M., et al., The influence of dog ownership on objective measures of free-living physical activity and sedentary behaviour in community-dwelling older adults: a longitudinal case-controlled study. BMC Public Health, 2017. 17(1): p. 496.
- 8. Mubanga, M., et al., Dog ownership and the risk of cardiovascular disease and death a nationwide cohort study. Scientific Reports, 2017. 7(1): p. 15821.

Sources of Images and Permission

- 1. Heart Disease Statistics: A Tsimane father teaching his boy to fish. Source: Photo RNW.org/Flickr
- 2. Heart Disease Statistics: Examples of intravascular ultrasound demonstrating plaque in different coronary arteries of teenagers. Permission: High Prevalence of Coronary Atheroclerosis in Asymptomatic Teenagers and Young Adults. Circulation, 2001, Author, E Murat Tuzcu, et al.
- 3. Heart Disease Statistics: Ancient Egyptian mummy being examined inside a CT scanner. Permission: Atherosclerosis in Ancient Egyptian Mummies, The Horus Study. JACC: Cardiovascular Imaging, Elsevier 2011, Author, Adel, H. et al.
- 4. Heart Disease Statistics: Example of extensive vascular clarification seen in an Egyptian mummy. Permission: Atherosclerosis in Ancient Egyptian Mummies, The Horus Study. JACC: Cardiovascular Imaging, Elsevier 2011, Author, Adel, H. et al.
- 5. Diet Chapter: Mediterranean Diet Pyramid. Permission: Oldways Preservation Trust.
- 6. Weight and Metabolism Chapter: Chart, Glycemic Index and Glycemic Load of Popular Foods. Source: http://nutriondata.self.com/topics/glycemic-index#ixzz2waw2XZx
- 7. Weight and Metabolism Chapter: Graph, High GI vs. Low GI foods. Source: https://www.linkedin.com/pulse/glycemic-index-vs-load-dr-harkirat-wilkhoo
- 8. Weight and Metabolism Chapter: Illustration of Kings. Permission: Marlena Agency Inc. Illustration by: Natalya Balnova
- 9. The Human Microbiome Chapter: Chart of Microbiota transplant. Permission: Fighting Obesity with Bacteria, Science, 2013, Author Walker & Parkhill.
- 10. The Human Microbiome Chapter: Open Biome Poop Bank Illustration, Source: http://www.freakingnews.com/The-Poop-Bank-Pictures-13277.asp.
- 11. The Human Microbiome Chapter: Picture of medication bottles, Fecal Microbiota. Source: Openbiome.org
- 12. Sleep Chapter: Sweeping brain picture, Permission: Cartoonstock, ID: mkan21
- 13. Sleep Chapter: Cerebrospinal fluid (blue) flows through the brain and clears out toxins through a series of channels that expand during sleep. Source: https://www.urmc.rochester.edu/labs/nedergaard.aspx
- 14. Sex and Cardiovascular Disease: Graph: Incidence of Coronary Artery Disease with Respect to Age and Erectile Dysfunction (ED) Status. Permission: A Population-Based, Longitudinal Study of Erectile Dysfunction and Future Coronary Artery Disease. Brant A. et al. Mayo Clinic Proceedings 2009.
- 15. Work and Your Heart Chapter: Picture "Frankly I Don't Give A Damn". Source: gelopsychedelico.com.
- 16. Understanding Coronary Artery Disease Chapter: Figure of Plaque Stabilization and Regression. Permission: Molecular Bases of the Acute Coronary Syndromes. Peter Libby, Circulation 1995.

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