

# Dietary Approaches to Longevity

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***Lifestyle Medicine is the therapeutic use of evidence-based lifestyle interventions to treat and prevent lifestyle related diseases in a clinical setting. It empowers individuals with the knowledge and life skills to make effective behavior changes that address the underlying causes of disease.***

American College of Lifestyle Medicine



## LIFESTYLE MEDICINE FOCUSES ON 6 AREAS TO IMPROVE HEALTH



# Lifespan

The length of time one lives

Increasing it = delaying the inevitability of death

Current average life expectancy in US in 2019

76 men

81 women

# Top 10 Causes of Death -2017

Heart disease

Cancer

Chronic lower respiratory diseases

Accidents (unintentional injuries)

Stroke (cerebrovascular diseases)

Alzheimer's disease

Diabetes

Influenza and pneumonia

Nephritis, nephrotic syndrome, and nephrosis

Intentional self-harm (suicide)













# Health span

The length of time that a person is healthy – not just alive

Avoiding (or delaying as long as possible) three categories of decline:

**Cognitive**

**Physical**

**Emotional**

*“While death is absolute and inevitable, a loss of the three elements of health span is not. They are **relative** (different people will have different thresholds of what constitutes decline), **analog** (they progress in stages rather than exist as an all-or-none switch), and most importantly, they are **not inevitable**.”*

Dr. Peter Attia

# How do we study longevity?

Basic science research

Epidemiology

Clinical studies

Centenarian studies



# Basic Science Research – Aging Genes

## IGF-1 and mTOR

Increased IGF-1 and mTOR promote aging and age-related diseases

Yeast, Flies, Mice with mutations in IGF-1 receptors have significantly enhanced longevity – 50% longer

Inhibition of mTOR by rapamycin extends life span in mice



IGF-1 and mTOR are assoc with increased protein intake in the diet

# Basic Science Research – Aging Genes

IGF-1

Laron Syndrome:

mutation in IGF-1 receptor  
leading to dwarfism

Very marked reduction of cancer and  
diabetes despite poor diet and  
lifestyle choices



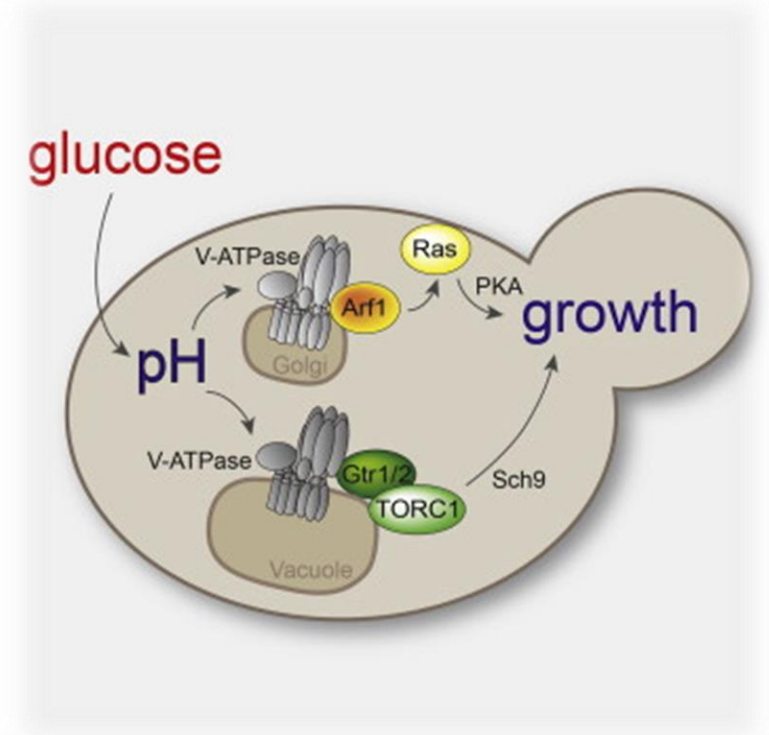
# Basic Science Research – Aging Genes

## PKA and RAS

PKA mutations extent lifespan in yeast, mice

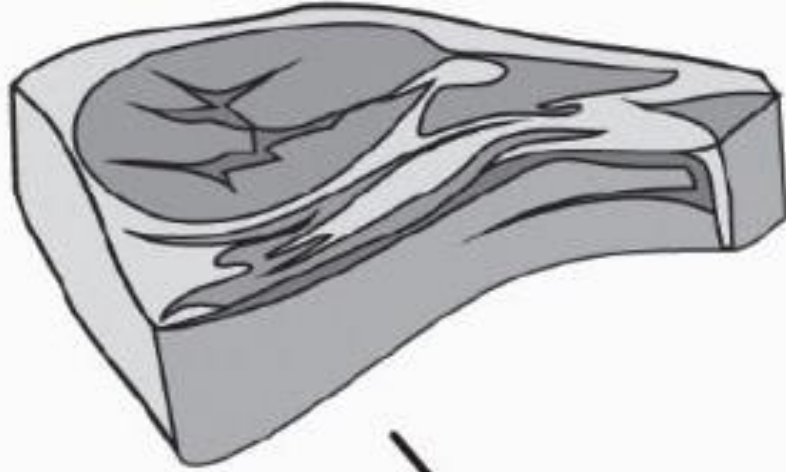
RAS mutations show improved resistance to oxidative stress in yeast, nematodes, fruit flies and mammalian neuronal cells

Sugar activates PKA and RAS





**Proteins**



**Sugar**



**GH-IGF-1, TOR-S6K**

**RAS-PKA**

**Aging + diseases (cancer, diabetes, etc.)**

# Epidemiology

JAMA Int. Med 2016 - prospective cohort study (131,342 Nurses Health and Health Professionals Follow-up Study Data

Higher animal protein intake = increased CV mortality

Higher plant protein intake = decreased CV and all-cause mortality (among those with 1 lifestyle risk factor)

Cell Metabolism 2014 – epidemiologic study (6,381 NHANES III data)

High levels of IGF-1 age 50-65 assoc with high protein diet

High protein intake before age 65 assoc with 75% inc risk of death and 4x inc risk of cancer

# Epidemiology

JAMA Int. Med 2013 – Adventist Health Study 2

Lower all cause mortality and some disease specific mortality for all forms of vegetarian diets (best for pescatarian)

AJLM 2017 Summary of Cohort Studies on dietary patterns

Significant reductions in cognitive impairment with Mediterranean diet (40%)



# Clinical Trials

NEJM 2018: RCT 7447 with high CV risk randomized to Mediterranean Diet with added olive oil, or with added nuts, or to low fat diet

Mediterranean diet decreased CV events v. low fat

3 RCTs 2013, 2015 demonstrating improvement in cognitive function and decreased cognitive decline with Mediterranean diet

Estruch et. al; N Engl J Med 2018; 378:e34

Martinez-Lapiscina et. al; J Nutr Healthy Aging 2013;17(6):544-52

Martinez-Lapiscina et. al; J Neurol Neurosurg Psych 2013 Dec;84(12):1318-25

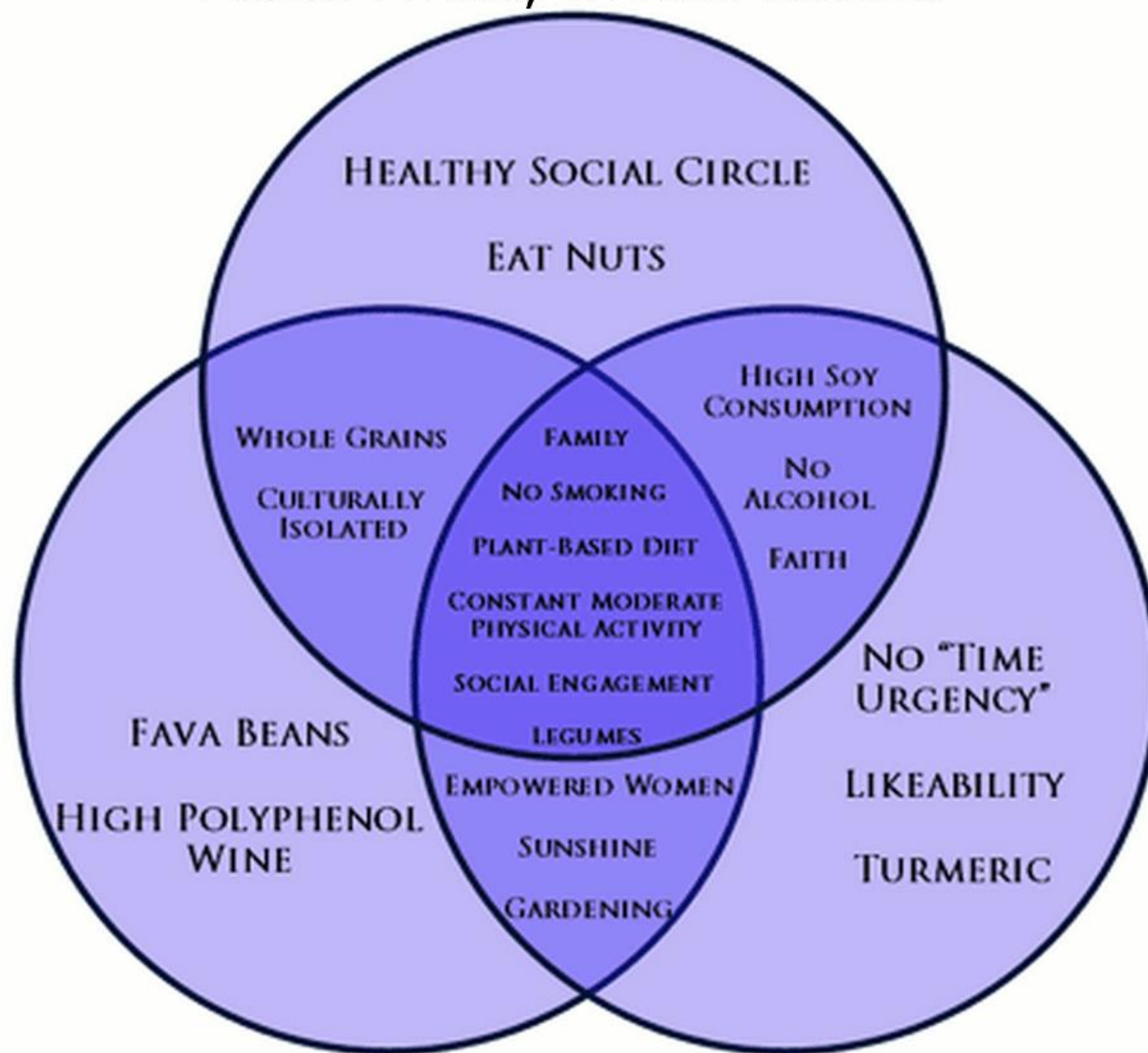
Valls-Pedret et. al; JAMA Int. Med. 2015 Jul;175(7):1094-1103

# Centenarian Studies – Blue Zones



# Loma Linda, United States

Sardinia,  
Italy



Okinawa,  
Japan

# Blue Zones Power 9<sup>®</sup>





Eat food.  
Not *too* much.  
Mostly plants.

Michael Pollan,  
In Defense of Food



# General Recommendations: Add These

## Vegetables: 5 servings/day

- (1 serving =  $\frac{1}{2}$  cup cooked or 1 cup raw)
- At least 1 serving of leafy greens recommended/day

## Fruits: 3 servings/day

- (1 serving = 1 cup or 1 medium piece or  $\frac{1}{4}$  cup dried)
- Preferably 1 serving of berries if possible

## Legumes: 1-2 servings/day

- (1 serving =  $\frac{1}{2}$  - 1 cup)
- Beans, peas, lentils

## Nuts and Seeds: 1-2 serving/day

- (1 serving = 1 Tablespoon)
- High omega – walnuts, flax, sesame, chia or hemp seeds

## Whole Grains: 1-2 servings/day

- (1 serving = 1 slice or  $\frac{1}{2}$  - 1 cup)
- Brown rice, whole wheat, quinoa, steel cut oats, old fashioned oat meal, millet, bulger



# General Recommendations: Limit These

**Meat/Animal Products:** up to 4 servings/week

- (1 serving = 4 oz, 1 cup dairy, 1 egg)
- White meat fowl, wild fish, lean grass-fed beef, eggs, dairy
  - AVOID: processed, cured, or barbequed meat

**Sat Fats/Oils:** 4 servings/week or less

- (1 serving = 1 Tablespoon)
- Refined oils, spreads, dressings

**Minimize All Caloric Beverages**

Recommend: water, seltzer, coffee, tea  
Alcohol (prefer wine): keep to 1-2 4oz servings/day



# Caloric Restriction

Long-term reduction in calorie intake

20-50% below habitual levels

Without malnutrition or nutrient deficiency

First posited as dietary intervention to promote longevity 80 yrs ago

Delays onset of age-related diseases in multiple species

yeast, worms, flies, fish, mice, rats and monkeys

# Caloric Restriction – Humans

Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy – CALERIE 1 and 2

## CALERIE 2:

218 young and middle aged; normal wt to mod overweight; 2 years

Randomized to 25% calorie restriction or usual diet

Lower total cholesterol, LDL-cholesterol, triglycerides, C-reactive protein, TNF-alpha, and blood pressure

HDL-cholesterol and insulin sensitivity increased

None achieved full 25% restriction- avg 12%



# Alternatives to Caloric Restriction - Fasting

The voluntary abstinence from food and drink – is an ancient tradition

Fasting flips a metabolic “switch”

Stimulates hormesis



# Alternatives to Caloric Restriction - Fasting

## Time-restricted eating

limiting food intake to certain hours of the day, without an overt attempt to reduce caloric intake

## Alternate-day fasting

abstaining from food and non-water beverages every other day, while eating normally on non-fasting days

## Prolonged fasting

multi-day, sometimes referred to as periodic fasting – fasting for more than 48 hours

# Time-restricted Eating

Limiting food intake to certain hours of the day, without an overt attempt to reduce caloric intake

“16:8”

Circadian effects of eating – zeitgeber

Studies:

- 3 meals in 6 hr window v. 12 hr – dec appetite and inc fat metabolism

- 8 hr window – 3% wt reduction compared to control

- Improved BP and circulating insulin levels

- Lower levels of grehlin, evening cortisol, increased expression of autophagy gene

# Alternate-day Fasting

Fasting every other day, while eating normally on non-fasting days

In a modified version of the alternate-day fast, participants can consume a small amount of food – approximately one-fourth of their optimal intake – on fast days

JAMA Intern. Med 2017 RCT – wt loss comparable to calorie restriction, less adherence

5:2

# Prolonged Periodic Fasting

Typically exceeds 48 hours up to 5 days

Promotes regenerative processes in the body:

**Apoptosis** - cellular self-destruct mechanism that rids the body of damaged or aged cells

**Autophagy** - sequesters protein aggregates, pathogens, and damaged or dysfunctional organelles into vesicles and then delivers them for destruction to release macromolecules such as proteins, fats, carbohydrates, and nucleic acids for energy and re-use



# Prolonged Fasting – Fasting Mimicking Diet

Fasting state:

- Lower IGF-1 levels

- Lower glucose levels

- Higher ketone body levels

- Higher growth factor inhibitor levels (IGFBP<sub>1</sub>)

Diet that is low in protein, sugar and high in healthy fats

Valter Longo, PhD. - PROLON



## The FMD

<b>Day 1</b> 1,100 calories	<ul style="list-style-type: none"><li>• 500 calories from complex carbohydrates (vegetables such as broccoli, tomatoes, carrots, pumpkin, mushrooms, etc.)</li><li>• 500 calories from healthy fats (nuts, olive oil)</li><li>• 1 multivitamin and mineral supplement</li><li>• 1 omega-3/omega-6 supplement</li><li>• Sugarless tea (up to 3 to 4 cups per day)</li><li>• 25 grams of plant-based protein, mainly from nuts</li><li>• Unlimited water</li></ul>
<b>Days 2–5</b> 800 calories	<ul style="list-style-type: none"><li>• 400 calories from complex carbohydrates (vegetables such as broccoli, tomatoes, carrots, pumpkin, mushrooms, etc.)</li><li>• 400 calories from healthy fats (nuts, olive oil)</li><li>• 1 multivitamin and mineral supplement</li><li>• 1 omega-3/omega-6 supplement</li><li>• Sugarless tea (up to 3 to 4 cups per day)</li><li>• Unlimited water</li></ul>
The above components can be divided between breakfast, lunch, and dinner, or they can be taken as two meals and a snack.	
<b>Day 6</b> Transition diet	For 24 hours following the end of the five-day FMD, patients should follow a diet based on complex carbohydrates (vegetables, cereals, pasta, rice, bread, fruit, etc.), and minimize the consumption of fish, meat, saturated fats, pastries, cheeses, milk, etc.

# Fasting Mimicking Diet Benefits

RCT with 100 patients, 5 days/mo FMD x 3 mo:

- Wt loss (mostly abdominal fat)

- Inc muscle mass

- Decreased BP, chol, triglycerides

- Decreased IGF-1 and CRP

3 mo after last cycle benefits persisted

Ongoing research around prevention and treatment of DM, CVD, Cancer, Dementia, Autoimmune disease



# Longevity Secret Sauce?

Eat food.  
Not *too* much.  
Mostly plants.

Michael Pollan,  
In Defense of Food

with

TRE?



# Resources for Patients

The Longevity Diet – Dr. Valter Longo

The Blue Zones – Dan Buettner

Undo It – Dr. Dean and Ann Ornish

In Defense of Food – Michael Pollan