# Gut Health for Healthy Aging

UW Retirement Association Lecture Series

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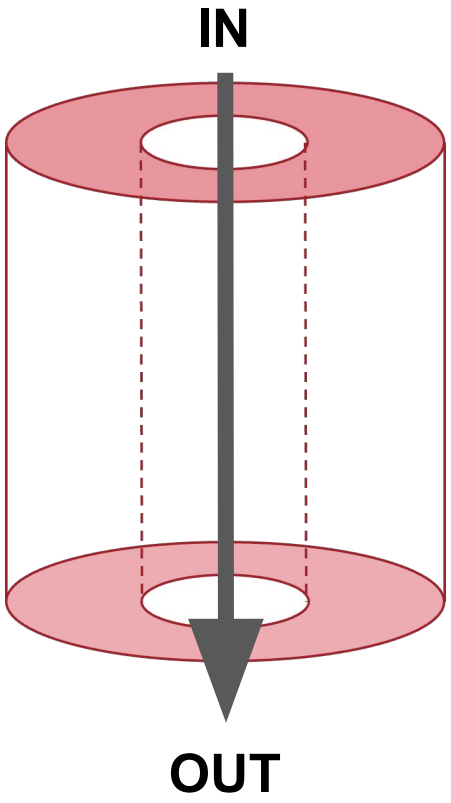
University of Washington

March 12, 2025

# Disclosures

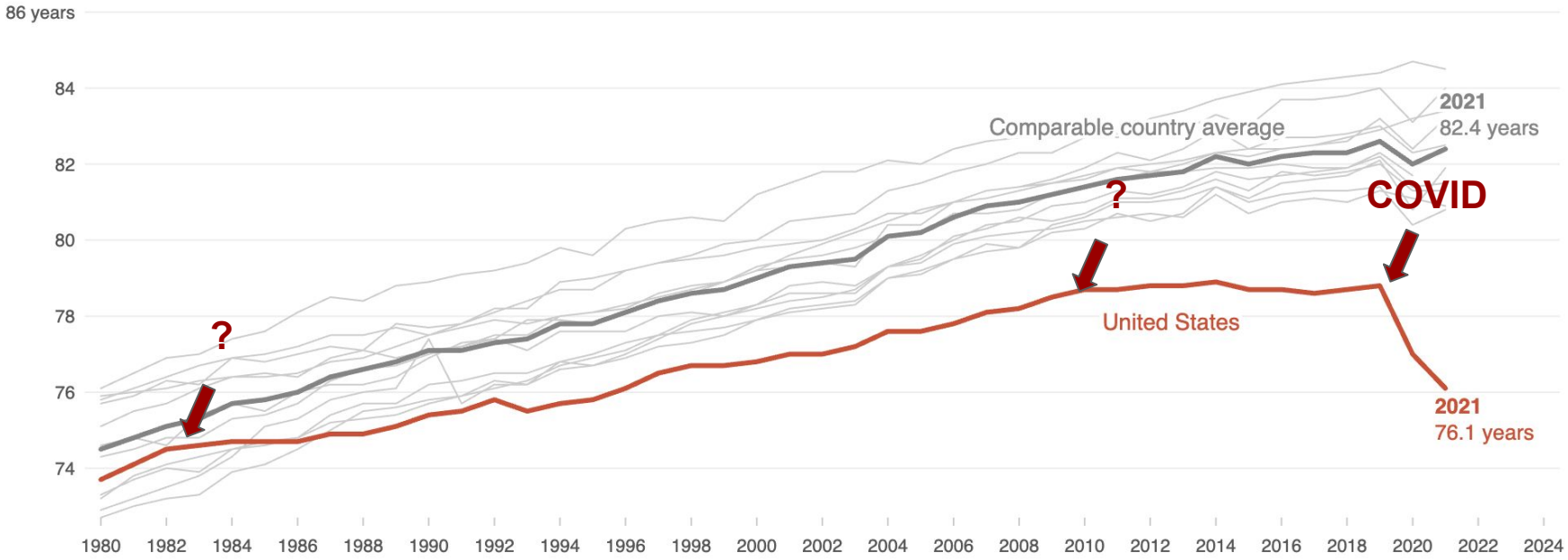
I consult for Supergut, BCD Biosciences, and Oobli

# What Will be Covered




- **Aging:**
  - Life expectancy ups and downs
  - Environmental contributors
  - Microbiome
- **Obesity/Metabolic Disease:**
  - Cause for Unhealthy Aging
  - Missing Food Factors
  - Missing Gut Microbiome Factors
- **Future Solutions:**
  - Food Sector
  - Smart Tech

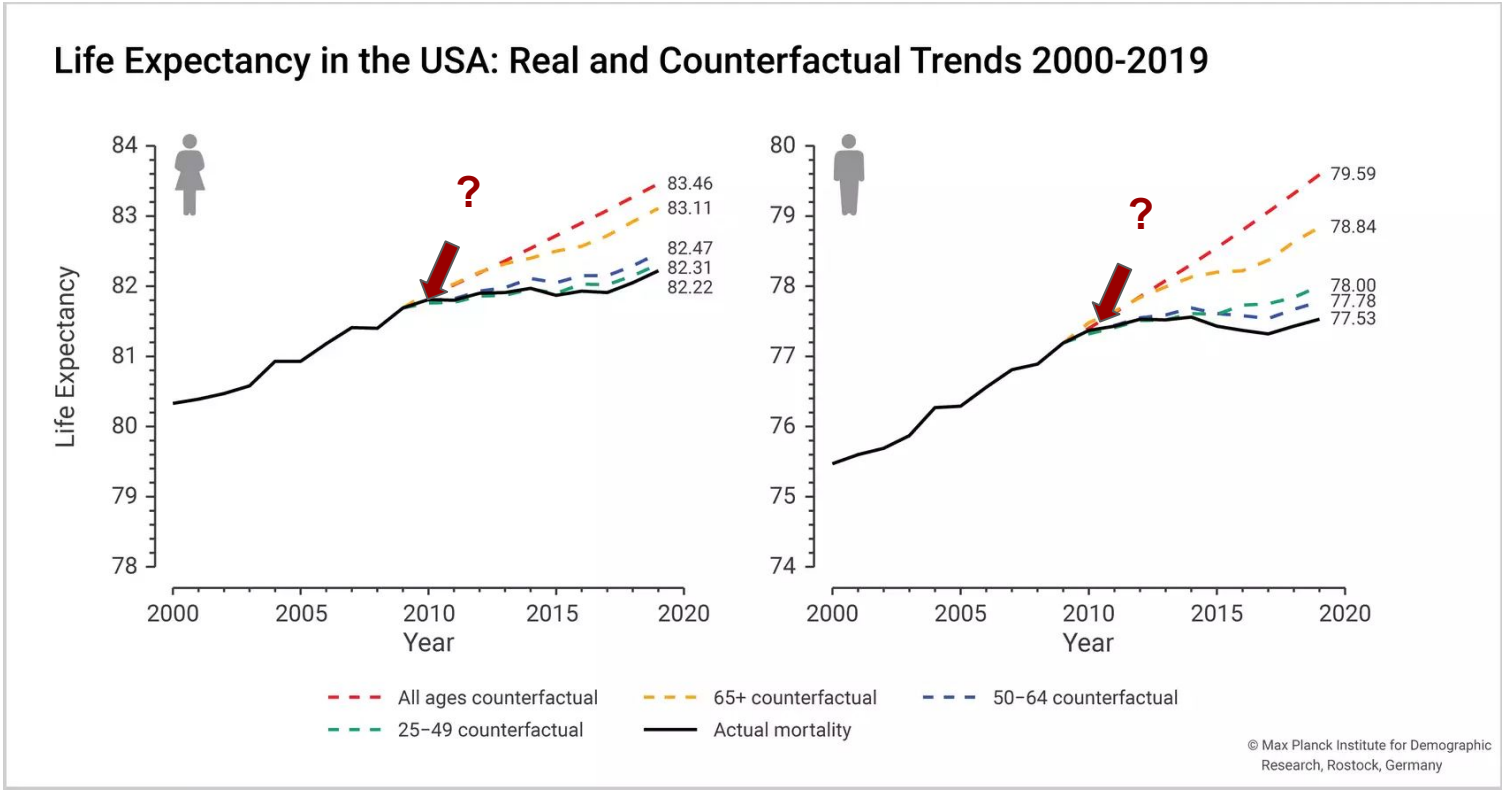
# Drop in United States Life Expectancy-All Ages




NPR: The Sad State of US Life Expectancy

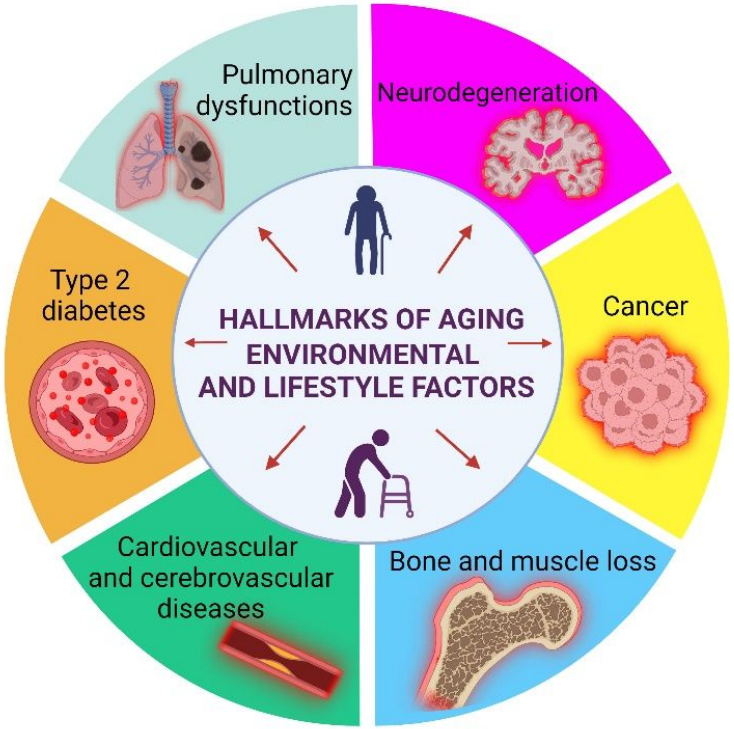
HealthSystemTracker.com

# Drop in US life Expectancy (65+)

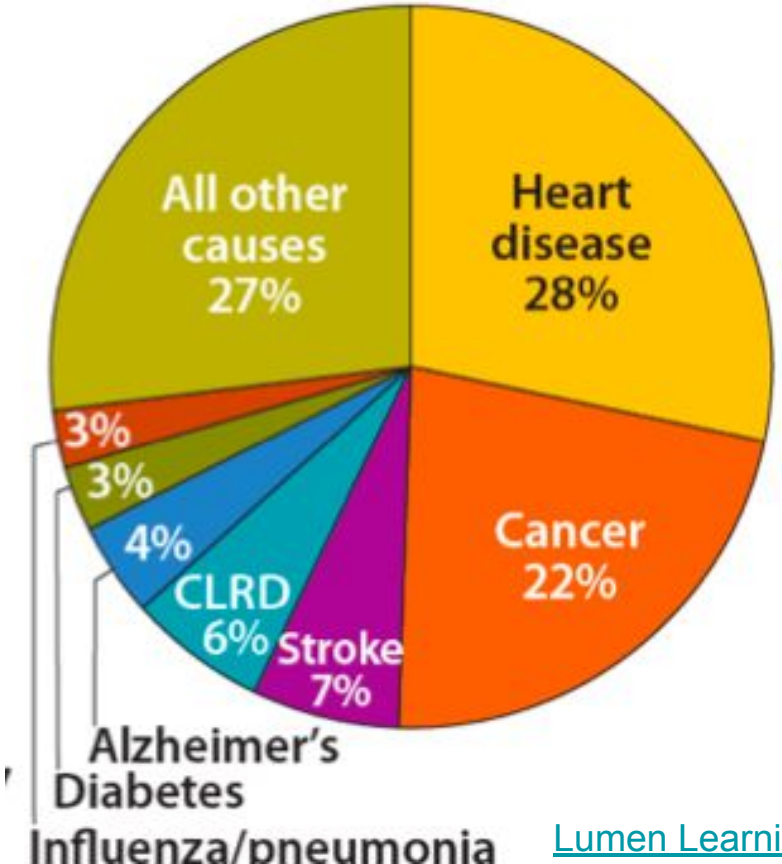



Abrams LR. PNAS 2023.

# Aging & Causes of Death in 65+

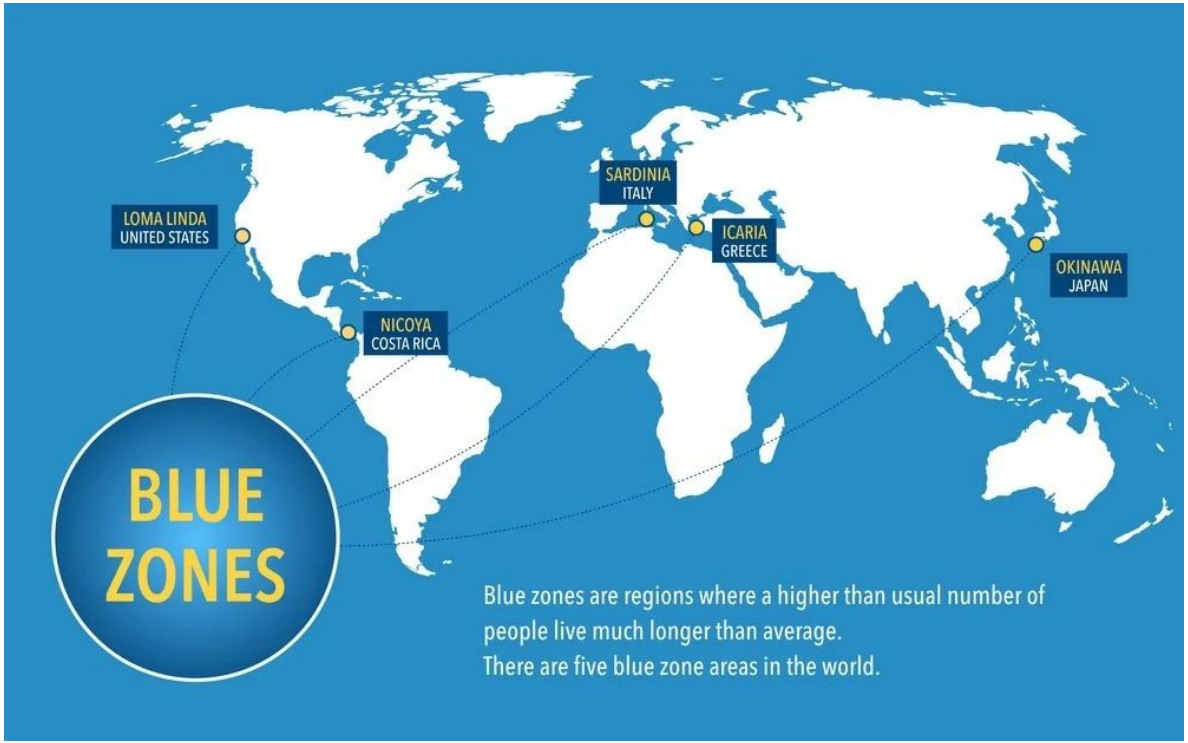



Chmielewski PP et al. Aging and Disease 2024




Lumen Learning

# Blue Zones & Healthy Aging to 100-Minimal Disease




Dimitrios Karamitros/Shutterstock.com

# BlueZone Lifestyle Factors


BlueZones.com

# Pillars of Health

## Movement

**Activity**
**Sedentarism**

istockphoto.com

## Mind

**Sleep & Mindfulness**
**Insomnia & Stress**


vectorstock.com

## Molecules

**Food**
**Toxin**


shutterstock.com

## Microbes

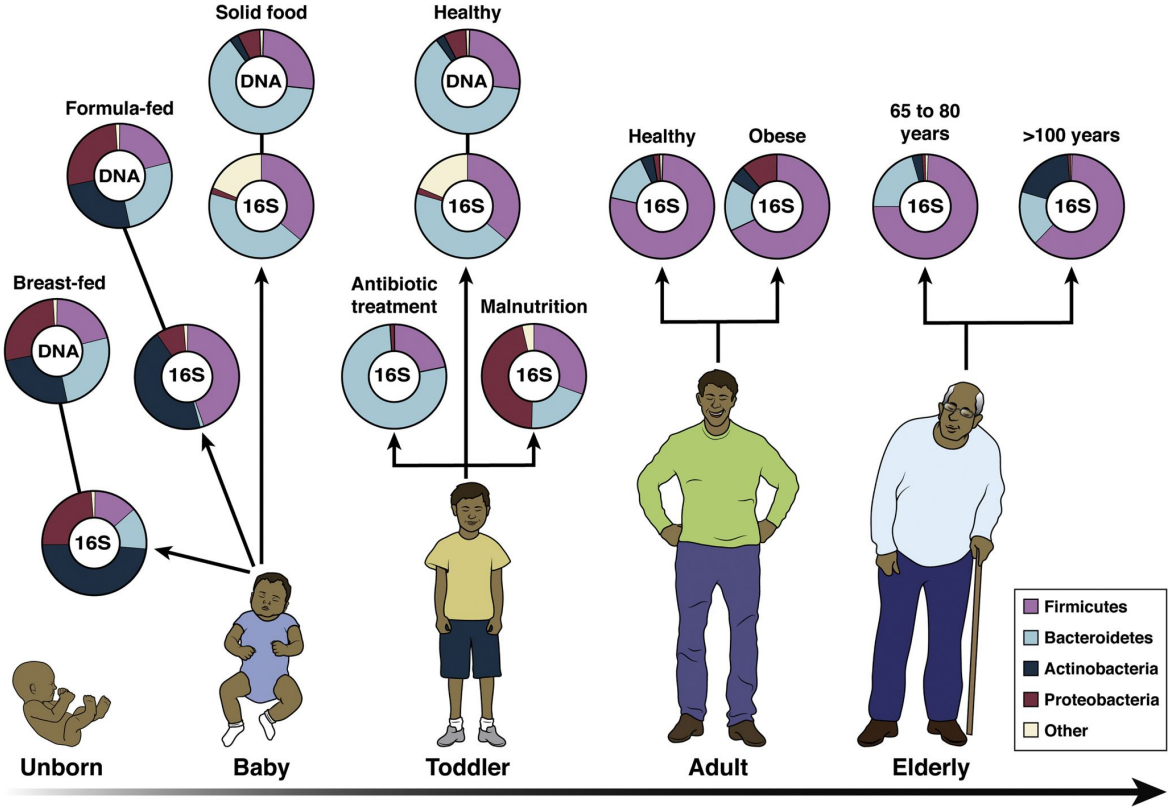
**Microbiome**
**Pathogen**

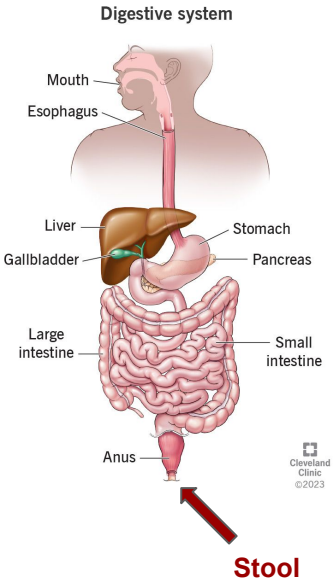
https://www.labiotech.eu

## Community

https://gutbites.org/

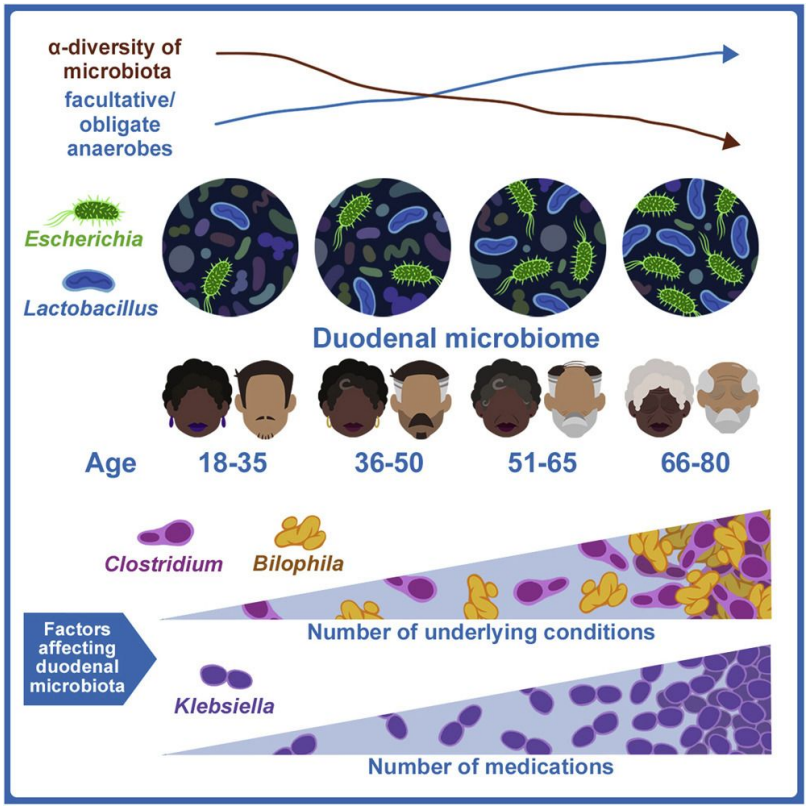
# Stool Microbiome With Age



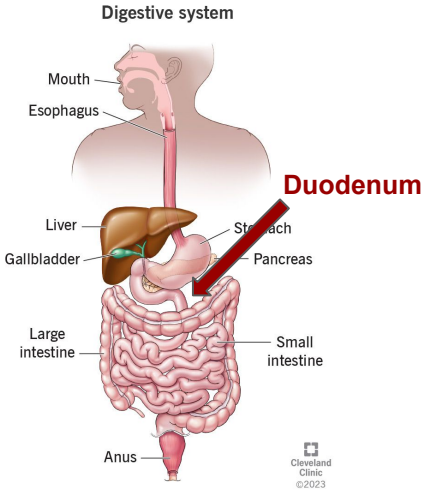




Harean JP 2021 Gastroenterology

# Duodenal Microbiome With Age

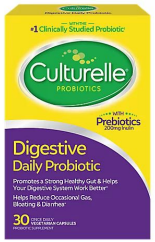



Leite G. et al. 2021

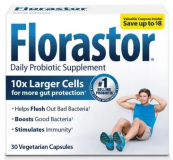


# Probiotics & Microbial Therapeutics

## Probiotics & Fermented Foods











*Lactobacillus ssp.*
*Saccharomyces ssp.*
*Streptococcus ssp.*
*Bacillus ssp.*

## Fecal Transplant & Live Bacterial Products

*Bifidobacterium ssp.*
*Akkermansia,*
*Clostridium ssp.*

VEDANTA BIOSCIENCES

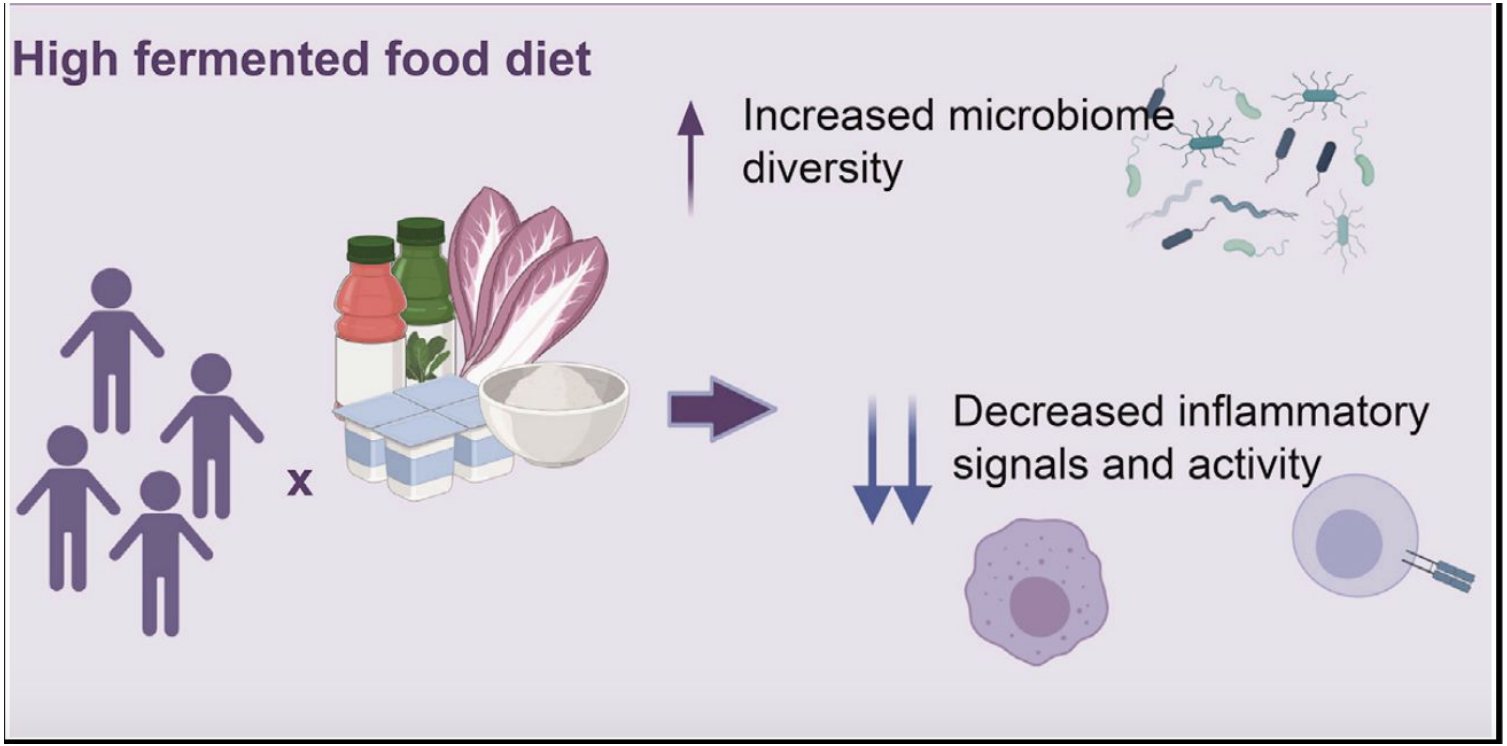
SERES THERAPEUTICS

FEDERATION BIO

Rebiotix®

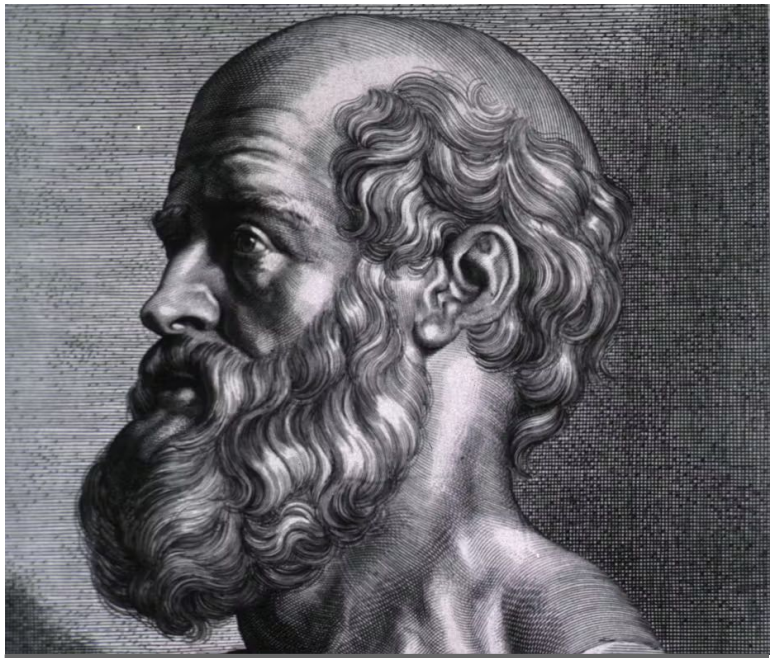
FINCH

# Fermented foods Decrease Inflammation



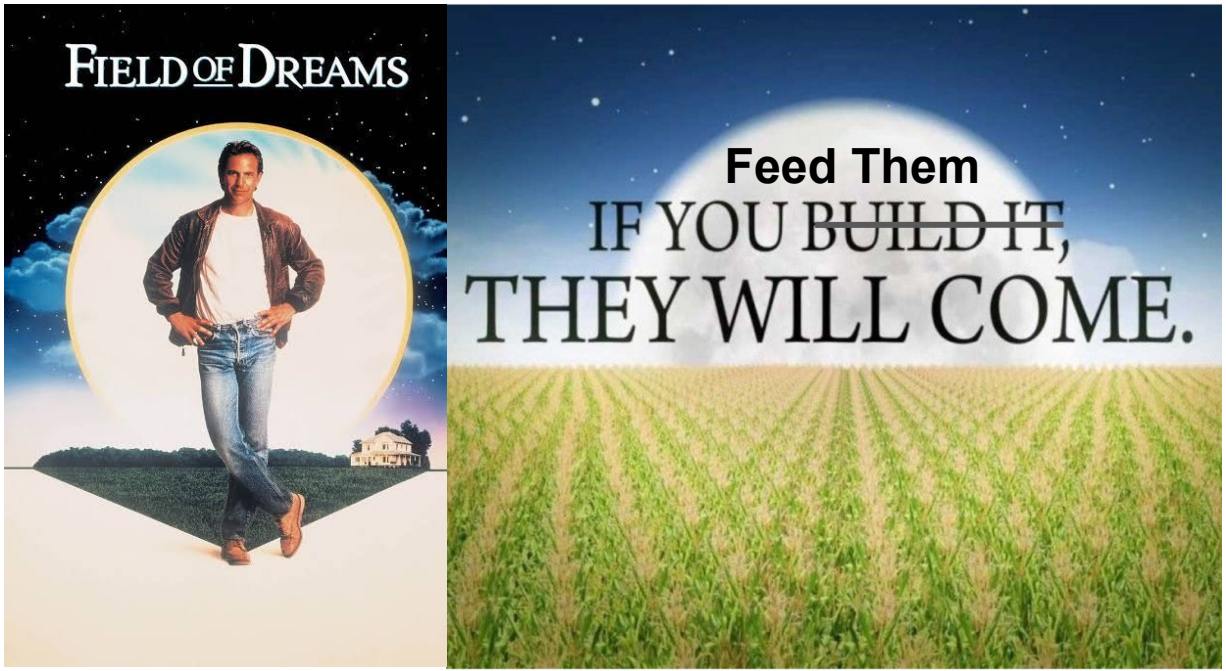

Wastyk HC. Cell 2021.

# “Let Food Be Thy Medicine”-Hippocrates (400 BC)



“Let Food Be Thy Medicine”
-Hippocrates (400 BC)

# If You Feed Them They Will Come

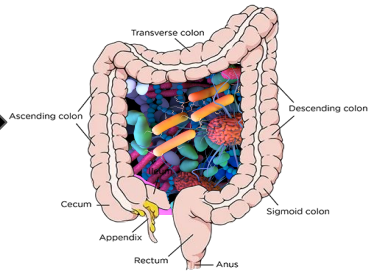


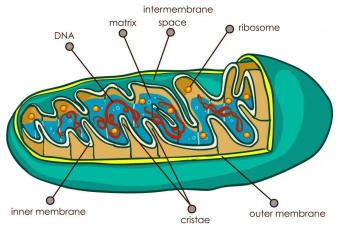
# Food-**Microbiome-Mitochondria**-Health Axis

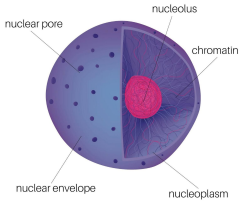
**Microbiome**
**Food Processor**

**Mitochondria**
**Energy Powerhouse**

**Nucleus**
**Command Center**




**Unhealthy Food→Depleted Microbiome → Dysfunctional Mitochondria → Disease**

| Metabolic Disease | Immune Disease | Frailty Disease | Neurologic Disease | Other Disease |
|---|---|---|---|---|
| • Obesity, Diabetes | • Autoimmune | • Osteopenia | • Alzheimer's | • Cardiovasc |
| • Stunting, Wasting | • Allergy | • Sarcopenia | • Mood | • Cancer |

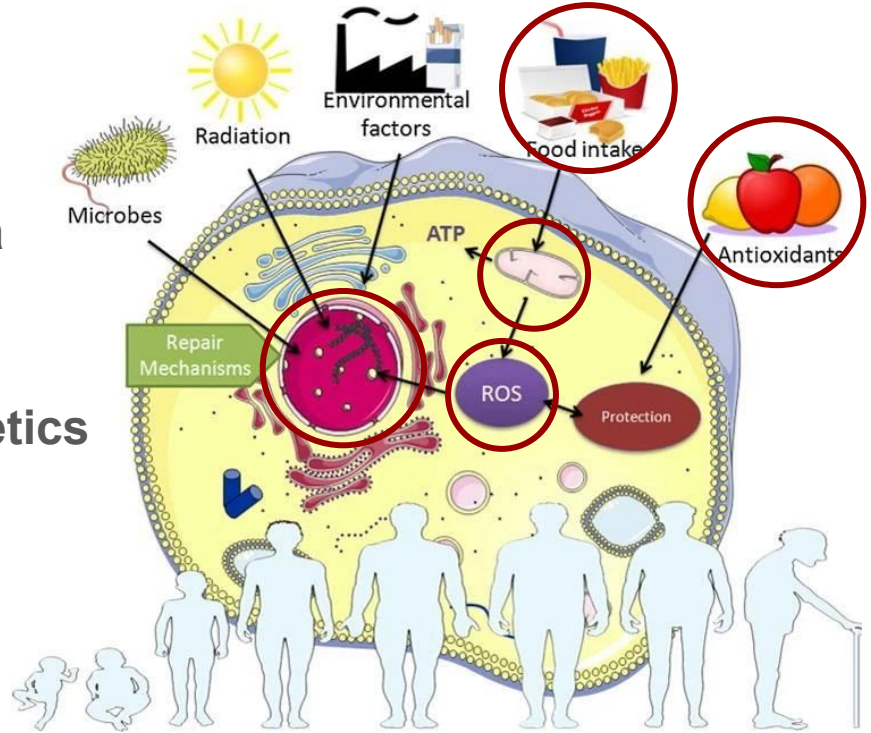
Damman CJ. Advances in Nutrition 2023

# Cellular Mechanisms of Aging

**Mitochondria**

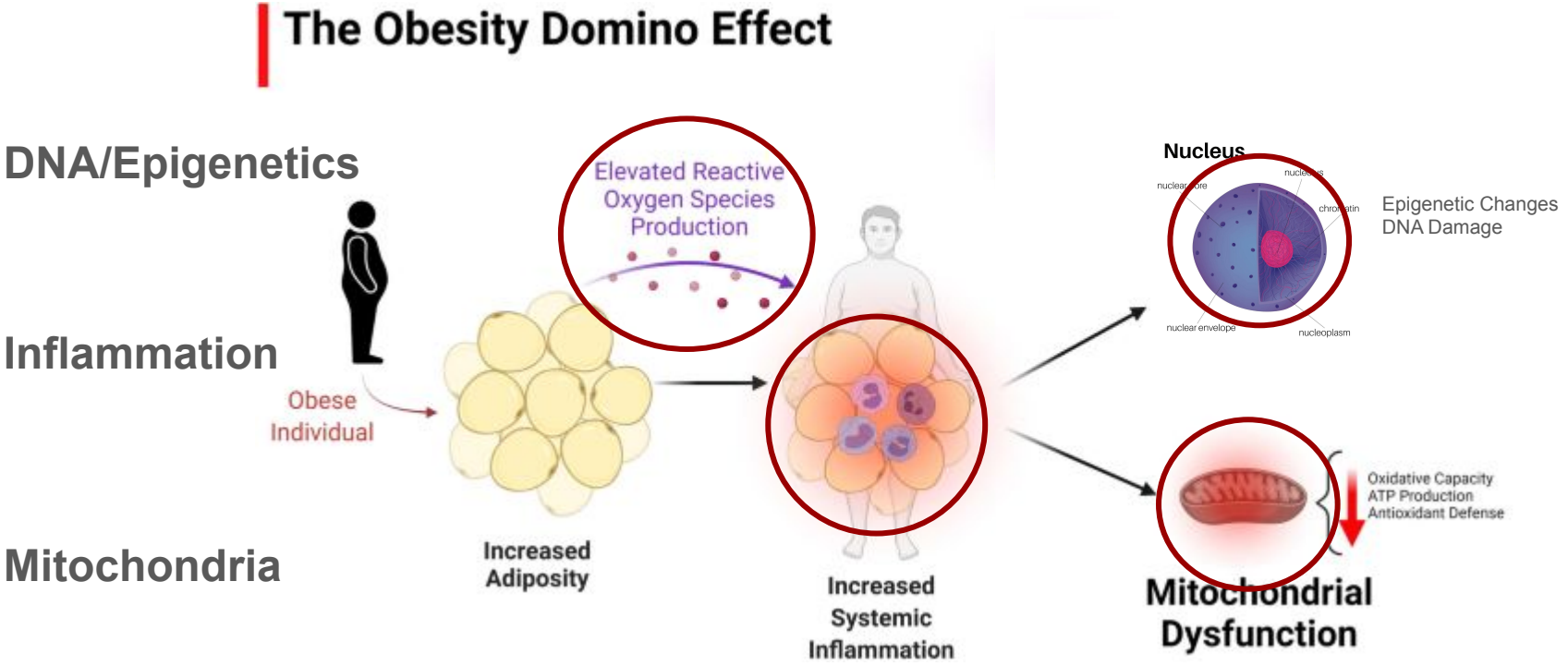
**Inflammation**

**DNA/Epigenetics**



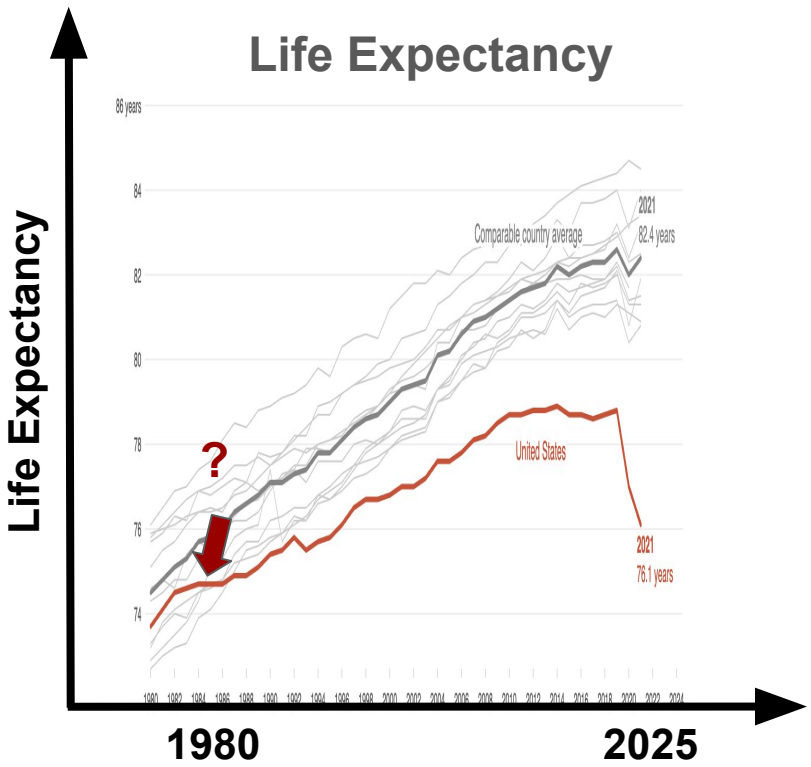

da Costa JP. Ageing Research Reviews. 2016

# Obesity - Premature Aging Phenotype

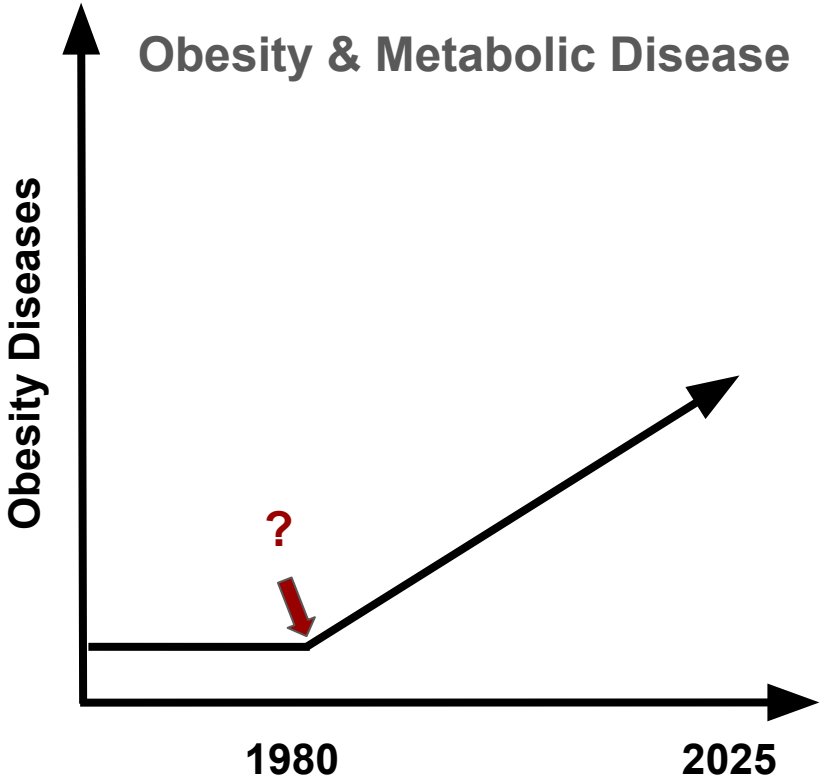



Nunan E. GeroScience. 2022

# Growing Burden of Obesity in the United States




HealthSystemTracker.com

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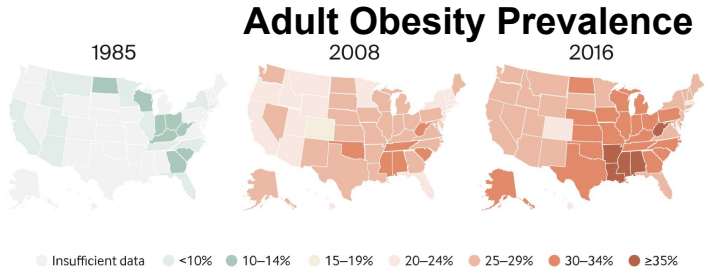
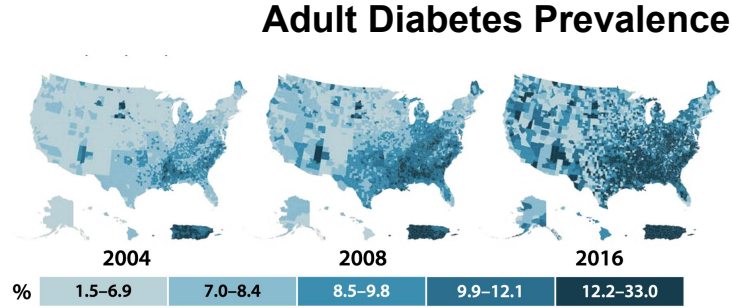
# Burden of Adult Obesity & Diabetes in the United States




https://www.commonwealthfund.org/blog/2018/rising-obesity-united-states-public-health-crisis

**Statistics from 2017:**

- 73% Overweight or Obese
- 42% Obese
  - Cost of $147B




https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

- 45% Pre-Diabetes or Diabetes
- 11% Diabetes
  - Cost of $327B

https://www.cdc.gov

# Different Diets -> Different Health

**Mediterranean**

Healthline.com

vs.

**Ultra-Processed**

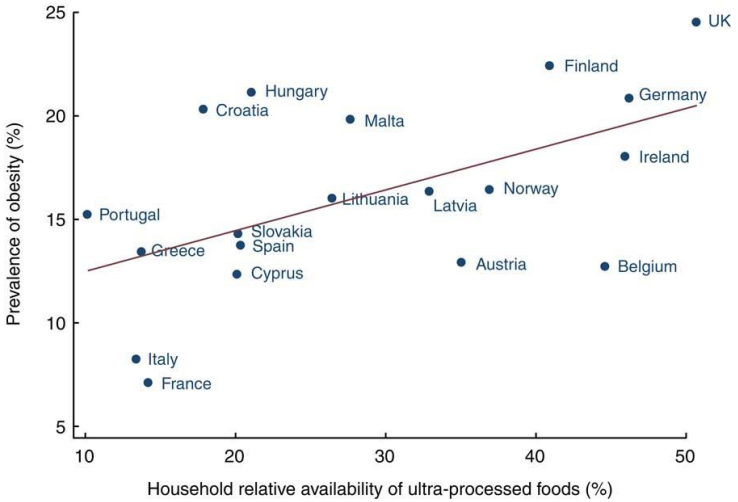
Healio.com

# Ultra-Processed Foods: Diabetes, Obesity, & Mortality

**Diabetes** 10% increase in ultra-processed foods ⇒15% higher risk of type 2 diabetes

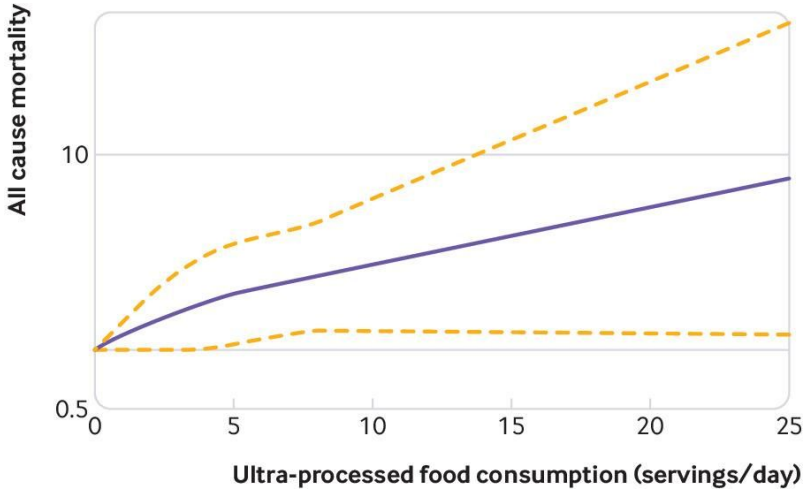
Srour B. JAMA Intern.Med. 2020.

**Obesity**




Monteiro C. Public Health Nutr. 2018.

**All-Cause Mortality**




Rico-Campa A. BMJ. 2019.

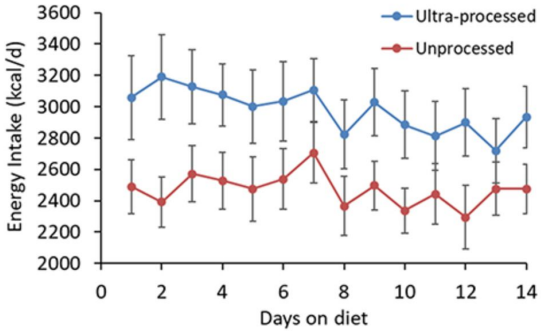
# Ultra-Processed Food Intervention & Weight Gain

**Ultra-Processed**

**vs.**

**Minimally-Processed**

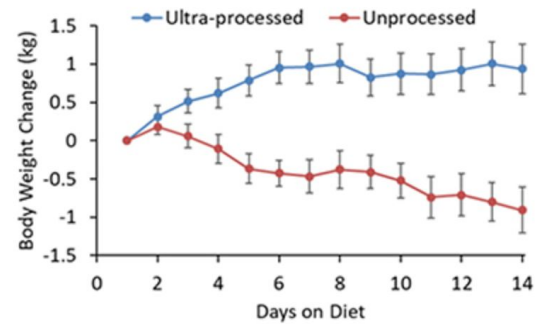
**Energy Intake**




## Study Design

- **Population:** 20 weight stable (BMI 27) subjects
- **Intervention:** 2 week cross-over: Ultra- vs. Minimally-Processed.
- **Control:** Isocaloric, iso-nutrient. Iso-fiber (46 g/day) - partially hydrolyzed guar gum added to liquids in ultra-processed diet. <u>Other factors not controlled for:</u> specific fibers, phytonutrients, fats.
- **Outcome:**
  - Significant difference in energy and sodium intake
  - Correlated with fat free mass and body weight.

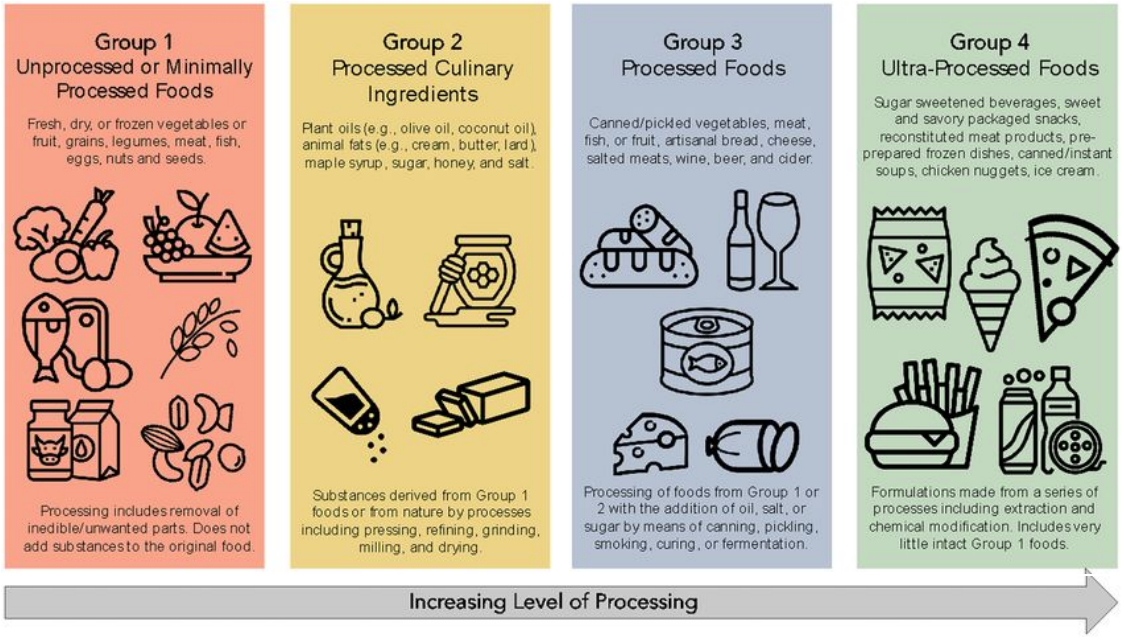
**Body Weight**




Hall K. Cell Metab. 2019

# What Are Ultra-processed Foods?

**NOVA Classification**

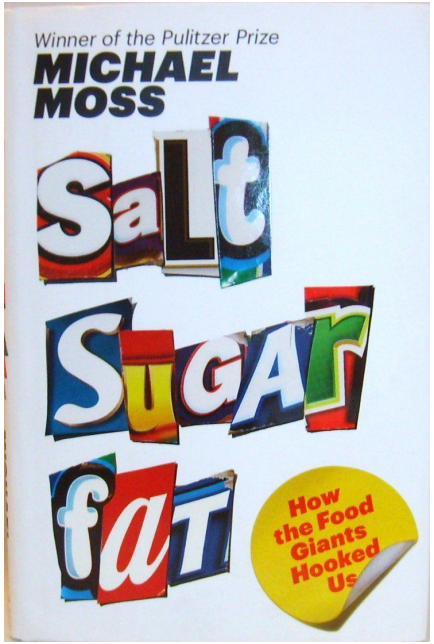



https://pubmed.ncbi.nlm.nih.gov/34677812/

https://www.fao.org/3/ca5644en/ca5644en.pdf

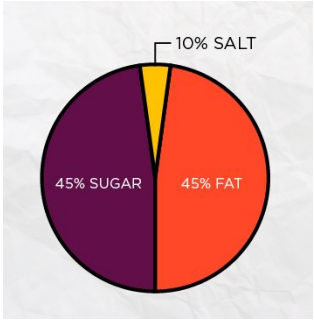
# What Is It About Ultra-Processed Foods?

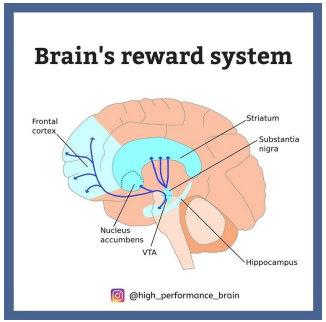
- **Added:** Too much sugar, salt, fat, and additives?



# What Is It About Ultra-Processed Foods?

- **Added:** Too much sugar, salt, fat, and additives?
- **Hyperpalatability:** Specific combinations of sugar, salt, & fat that can be addictive?






https://www.fao.org/3/ca5644en/ca5644en.pdf https://www.frontiersin.org/articles/10.3389/fnut.2022.821657/full

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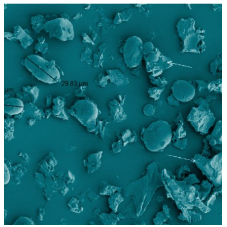
- **Disrupted Matrix:** Cell & food ultrastructure gone and calories that are too easily absorbed?



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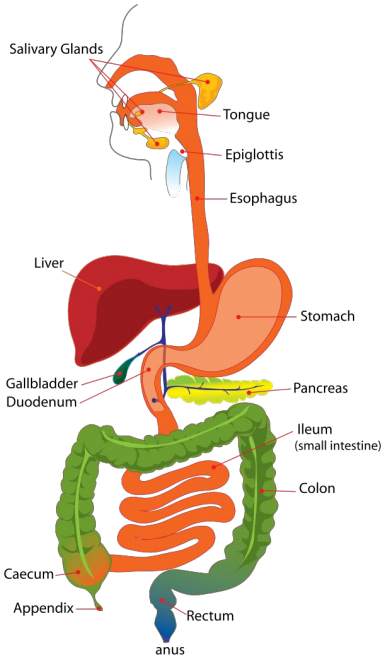


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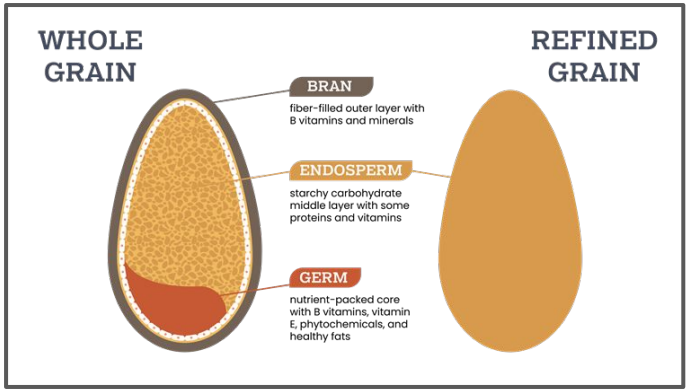
- **Disrupted Matrix:** Cell & food ultrastructure gone and calories that are too easily absorbed?
- **Missing:** Missing fibers, phytonutrients, bioactive fats?

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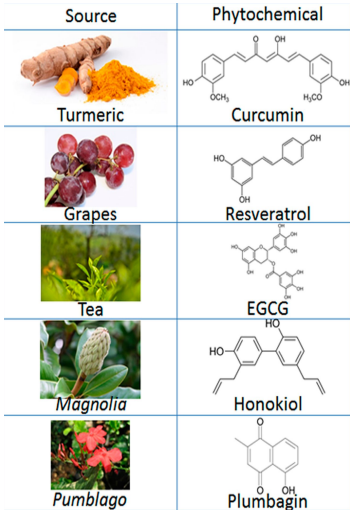
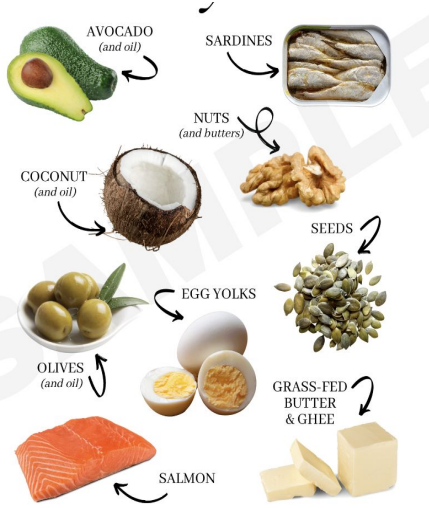
# The Phonetic “F”’s of Food

## Fibers


## Phenols




## Fat Bioactives




## Ferments

# Four Phonetic F Foods & Blue Zones

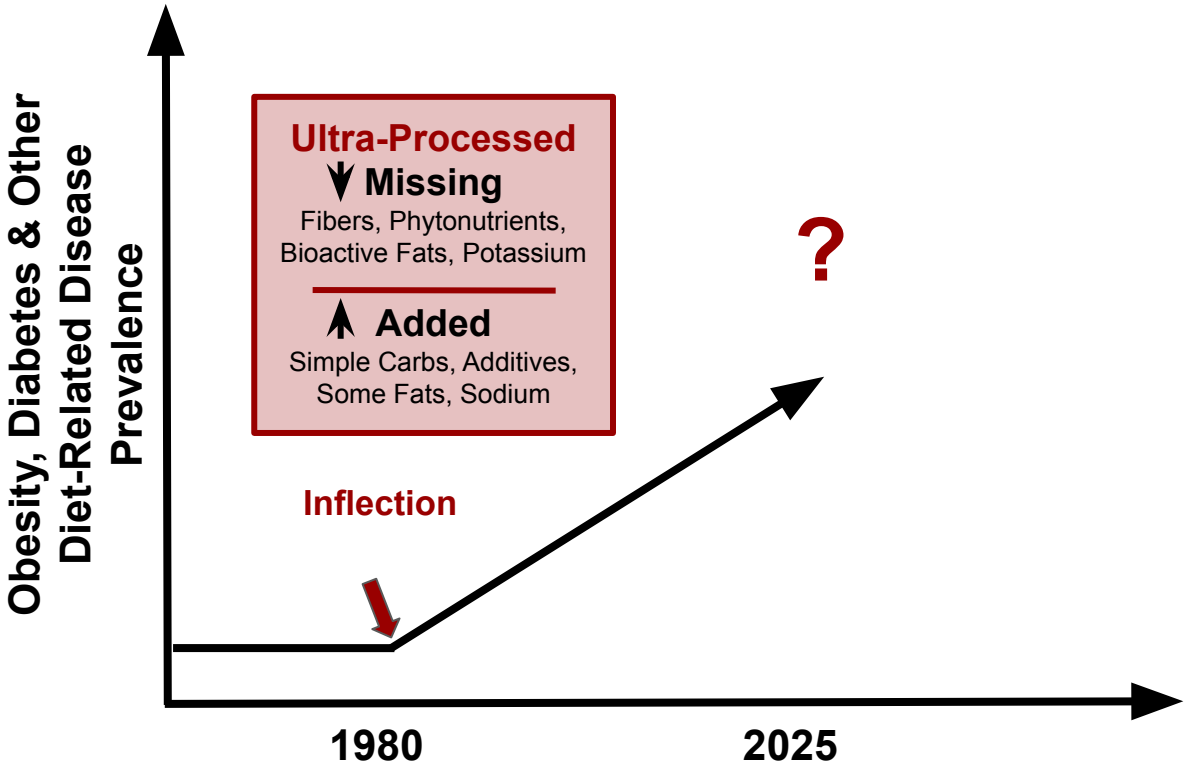
## Blue Zones "4F" Foods for Microbiome & Mitochondria

| Blue Zones | Fiber | Phenols* | Fats (Omega-3's) | Ferments |
|---|---|---|---|---|
| Mediterranean<br>Icaria, Greece<br>Sardinia, Italy | Beans (fava, lentils, chickpeas)<br>Potatoes<br>Barley & Whole Grains | Herbs & Herbal Teas<br>Grapes & Fruits<br>Olives & Vegetables | Fish (anchovies, shellfish)<br>Olive oil<br>Nuts<br>Pasterual Beef, Lamb, Pork (occasionally) | Balsamic Vinegar<br>Olives<br>Red Wine<br>Yogurt & Cheese |
| Okinawa, Japan | Purple Sweet Potatoes<br>Brown Rice<br>Soybeans | Purple Sweet Potatoes<br>Green/herbal tea<br>Turmeric, Ginger<br>Bitter Melon, Vegetables | Fish<br>Seaweed<br>Grass-seaweed-fed pork (occasionally) | Rice Wine Vinegar<br>Miso<br>Nato<br>Sake |
| Nicoya, Costa Rica | Black Beans<br>Squash/Yams<br>Corn Tortillas<br>Plantains/Yuka | Black Beans<br>Coffee/Herbal tea<br>Turmeric, culantro, spices<br>Fruits & Vegetables | Fish<br>Pastoral Beef, Pork, Chicken & Eggs (moderate) | Coffee<br>Cacao<br>Coyol (Palm) Wine<br>Cuajada cheese |
| Loma Linda, California | Oatmeal & Whole Grains<br>Beans | Fruits & Vegetables | Avocado<br>Nuts & seeds | Ferments avoided |
| What's in Common? | Beans, Potatoes & Whole Grains (esp. oats & barley) | Teas, Coffee & Cacao<br>Turmeric, Herbs & Spices<br>Fruits & Vegetables | Olives & Avocados<br>Nuts & seeds<br>Fish & Free-Range Meats | Vinegars & Drinks<br>Fermented Vegetables, Beans & Dairy |

*Phonetic F

GutBitesMD: Hangry Microbiomes

# But How Do These Components Affect Health?

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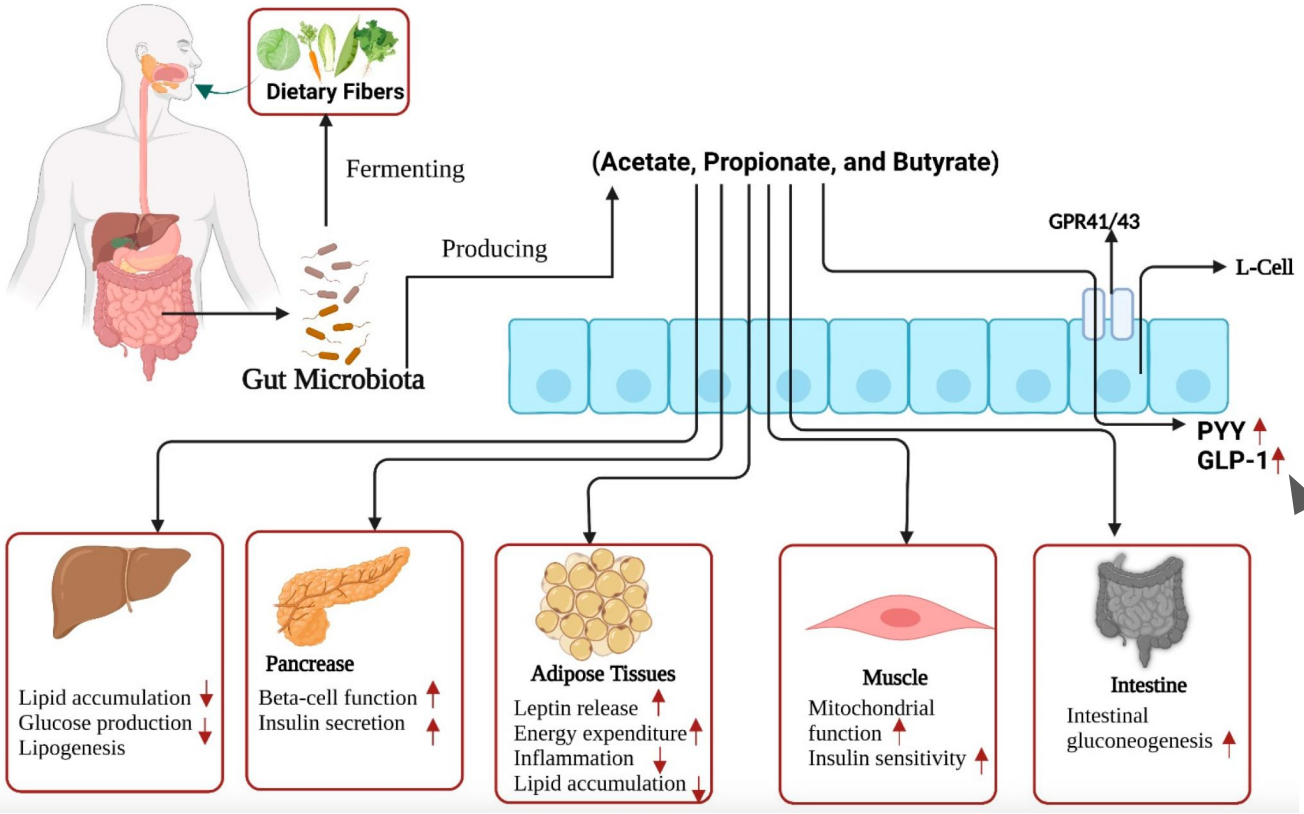
# Fiber→Butyrate



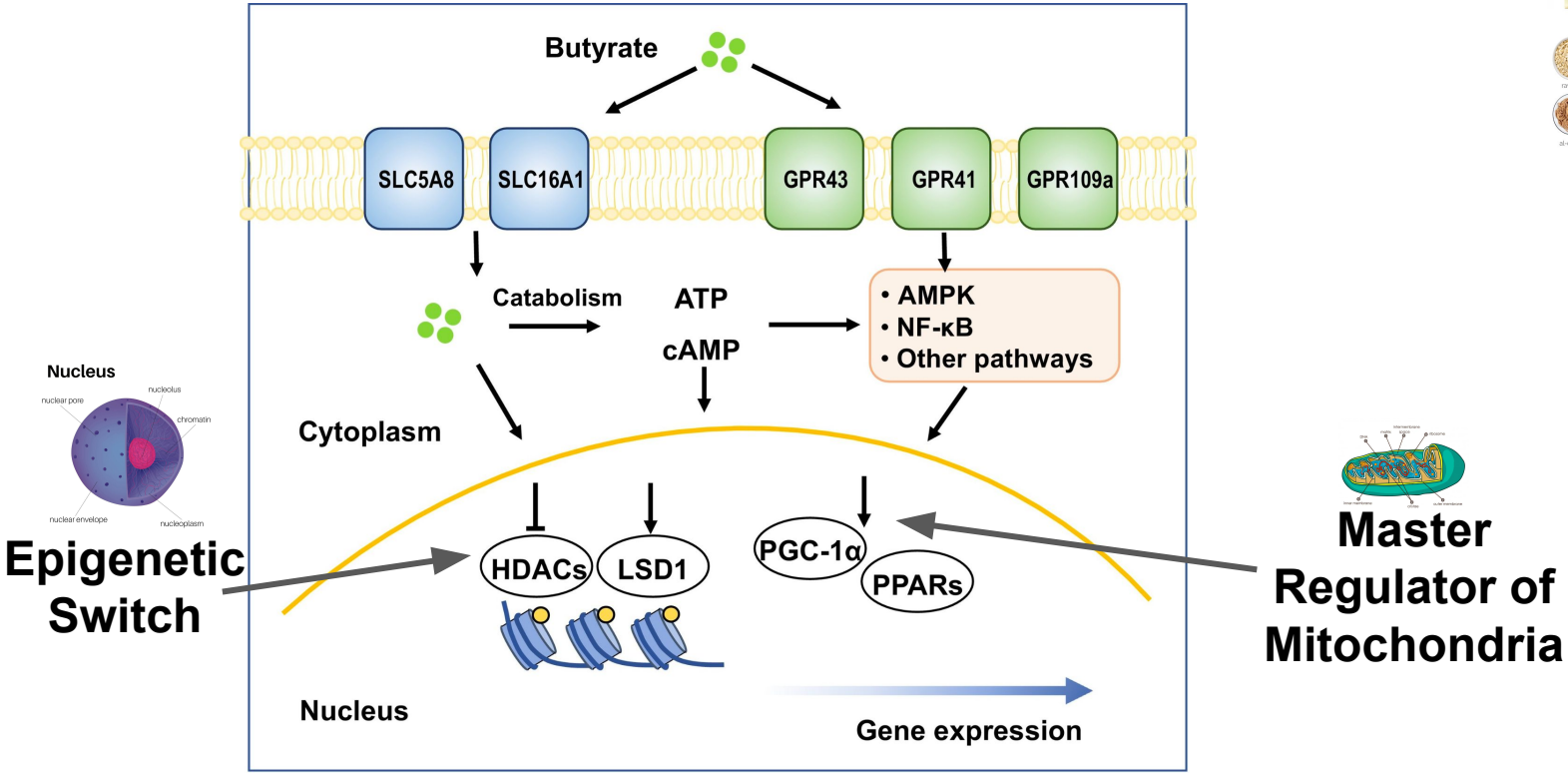

Fiber


**Wegovy & Ozempic Natural Analogue**

Mazhar et al. Foods 2023.

Fiber

# **Fiber→Butyrate:** HDACi, PGC-1, & Mitochondria

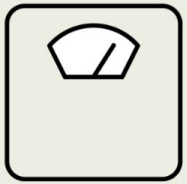

Zhang L. et al. Trends in Endocrin. & Metab. 2021

# **Butyrate** and Pediatric Obesity

## RCT: Therapeutic Effects of Butyrate on Pediatric Obesity

### POPULATION

**23 Males, 31 Females**



Pediatric patients with obesity

**Mean age, 11 y**

### INTERVENTION

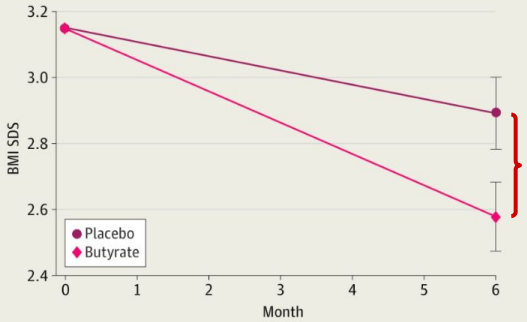
**54** Patients randomized

**27 Butyrate group**
Standard care for pediatric obesity plus 20 mg/kg of body weight/d of sodium butyrate orally

**27 Placebo group**
Standard care for pediatric obesity plus placebo

### FINDINGS

In an intention-to-treat analysis assuming that patients lost to follow-up had reached the primary outcome, children treated with butyrate had a higher rate of BMI decrease ≥0.25 SDS at 6 mo than placebo




**Proportion in butyrate group with primary outcome:**
0.96 (95% CI, 0.89-1.03)
**Proportion in placebo group with primary outcome:**
0.56 (95% CI, 0.37-0.74)
**Absolute benefit increase:**
40% (95% CI, 21%-61%); $P < .001$

### SETTINGS / LOCATIONS

**A university tertiary center for pediatric nutrition in Italy**

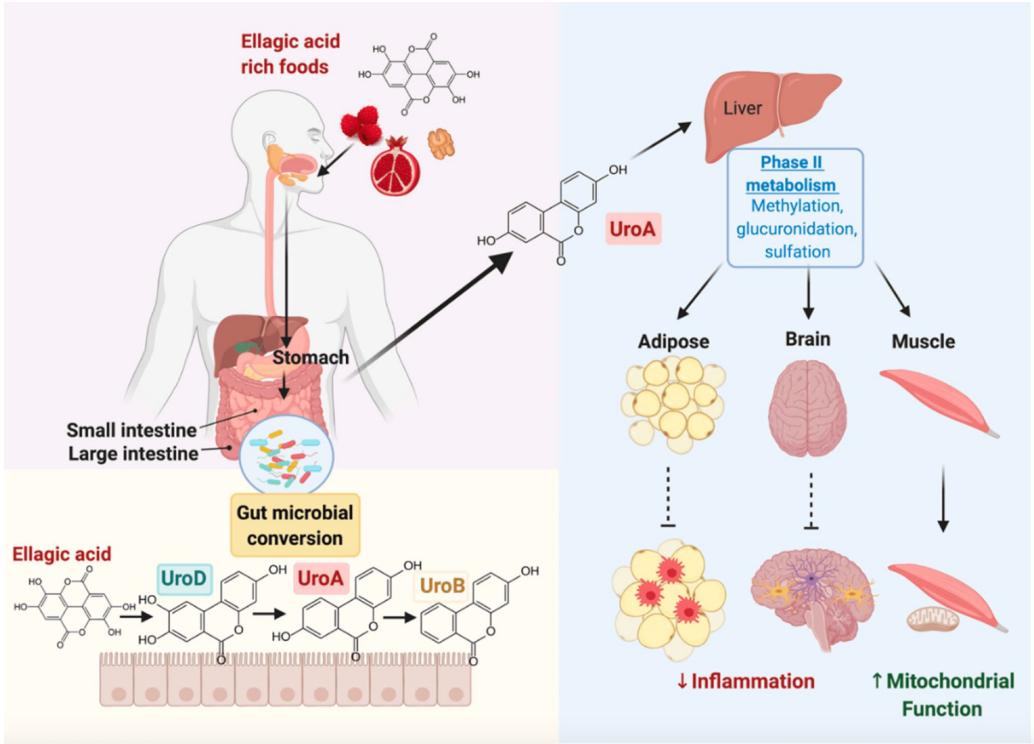
### PRIMARY OUTCOME

Body mass index (BMI) decrease of ≥0.25 BMI SD score (SDS) after 6 mo of intervention

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799197

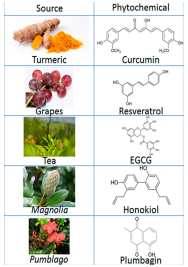
**Fiber**


# Phenols→Urolithin A



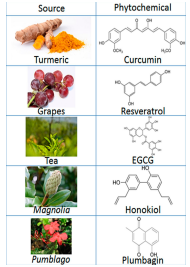

Toney A. Biomedicines 2021.

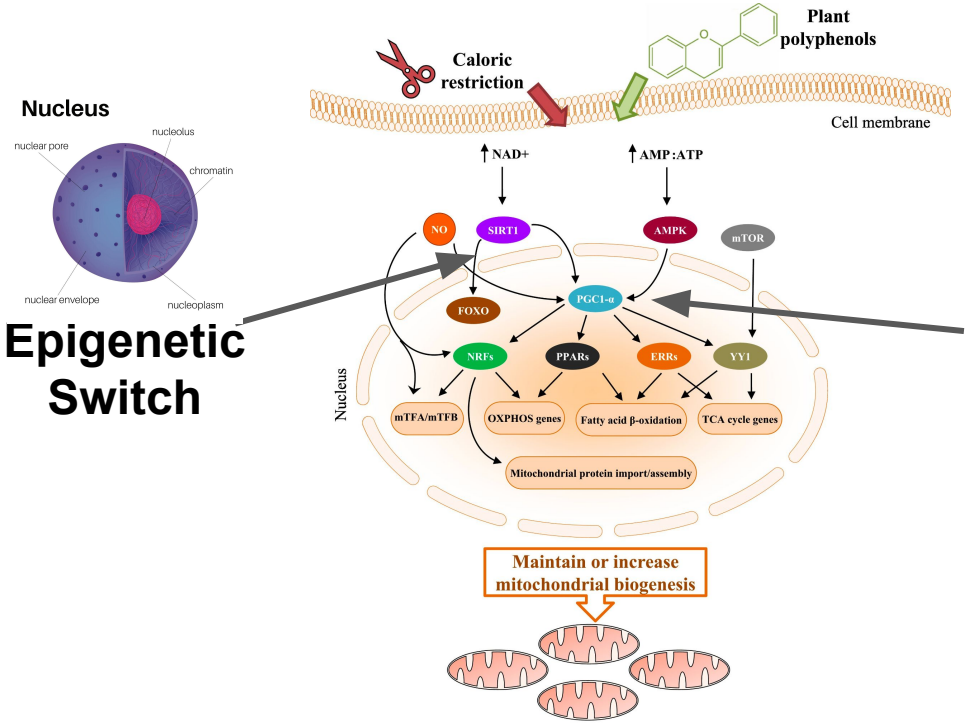
Phenols

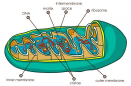


Phenols

# **Phenols→Urolithin:** SIRT1, PGC1-alpha



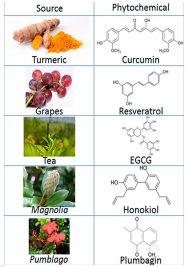



**Master Regulator of Mitochondria**

Davinelli S. et al. Trends in Endo. & Metab. 2020.

Phenols




# **Urolithin A** & Muscle Endurance

**RCT: Effect of Urolithin A vs Placebo Supplementation on Muscle Endurance and Mitochondrial Health in Older Adults**

**POPULATION**

**16 Men, 50 Women**

Healthy adults 65-90 y old with average physical performance and mitochondrial function

**Mean age, 71.7 y**

**INTERVENTION**

**60** Participants randomized and analyzed

**30 Placebo**
4 Oral placebo softgels of matching size daily

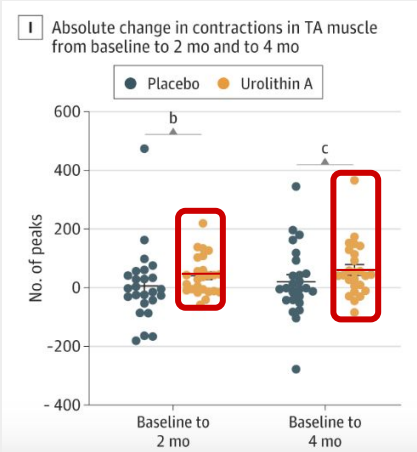
**30 Urolithin A**
4 Oral urolithin A 250-mg softgels daily

**SETTINGS / LOCATIONS**

**2 Medical centers in Seattle, WA**

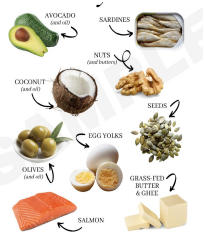
**PRIMARY OUTCOME**

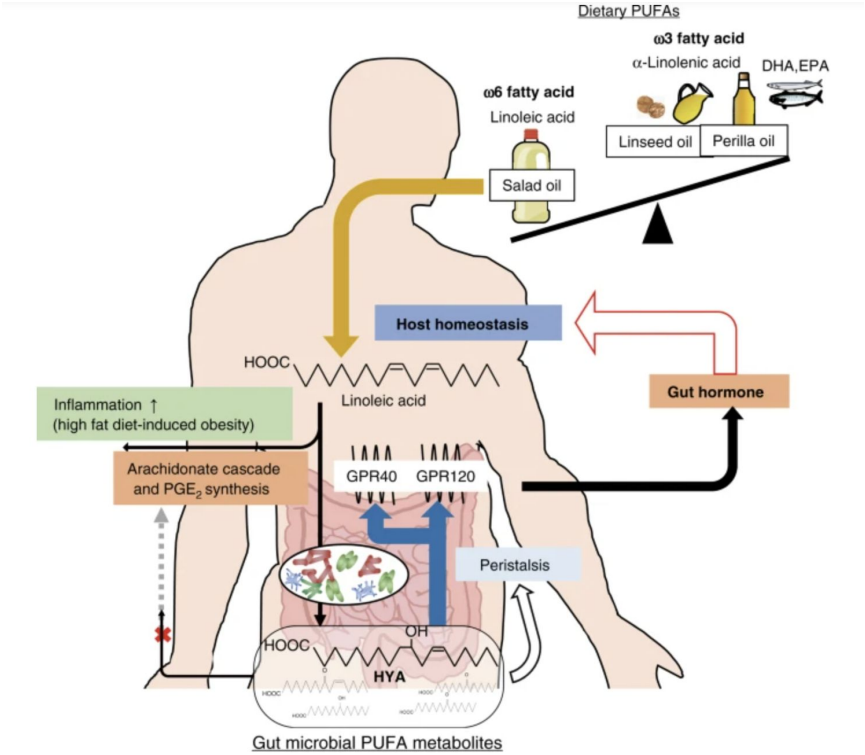
Change from baseline to 4 mo in 6-min walk distance (6MWD), as assessed by a 6-min walk test during which participants walked laps around a 15-m course and total distance walked after 6 min was recorded in meters




Liu s et al. JAMA 2022.

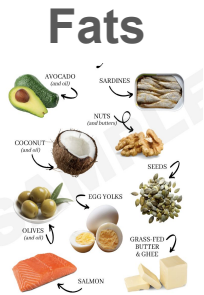
# Fat->Conjugated Linoleic Acid

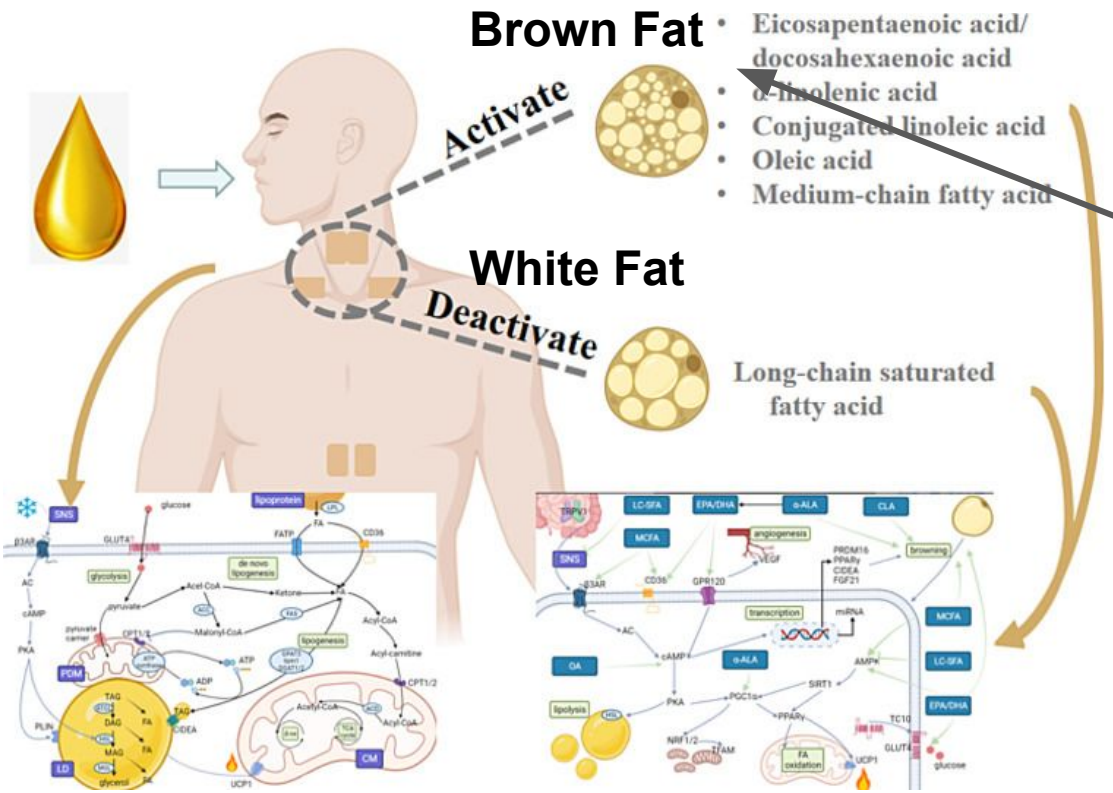


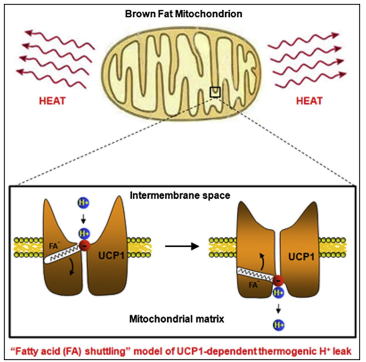

Miyamoto et al. Nat Commun. 2019.

# **Fat->Conjugated Linoleic Acid**: Thermogenesis



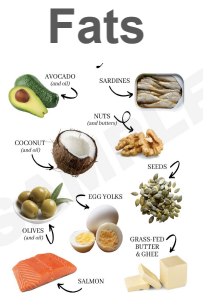



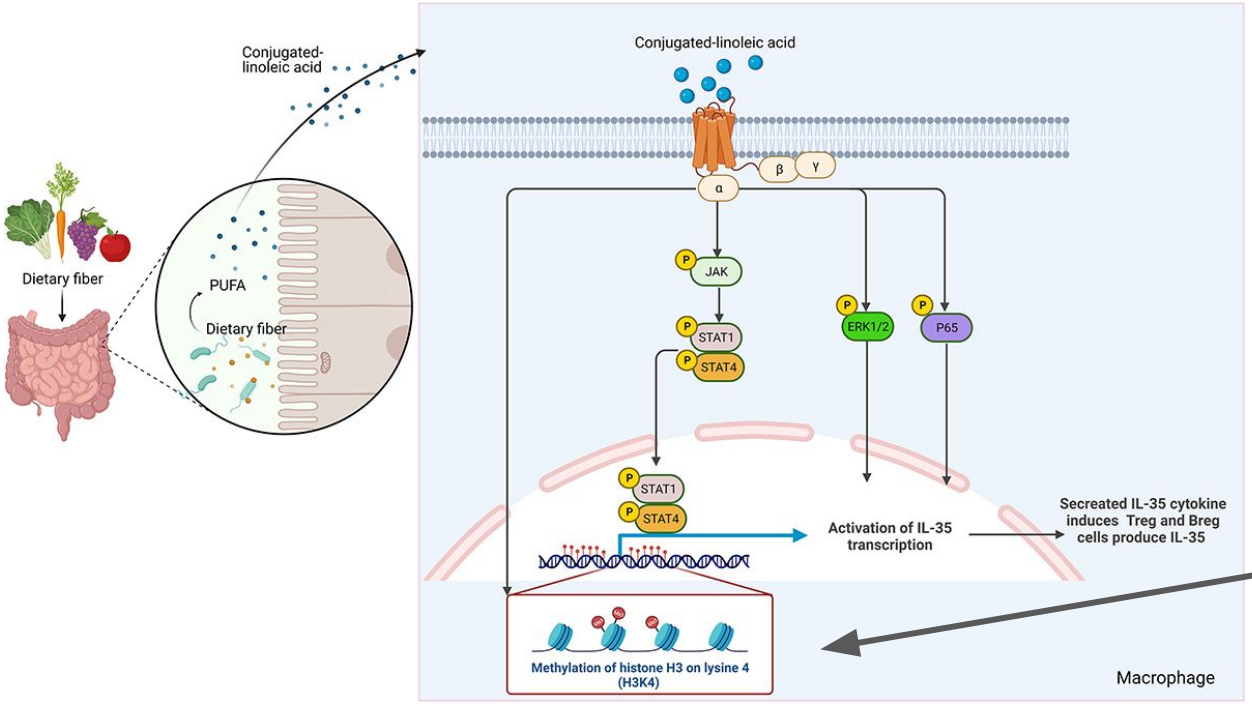

**Increase in Browning of White Fat & Thermogenesis**

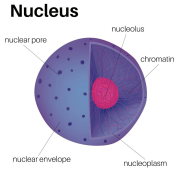



Jia M. et al. Life Sciences 2023.

# **Fat->Conjugated Linoleic Acid**: Epigenetics



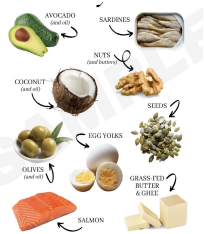




**Epigenetic Switch**

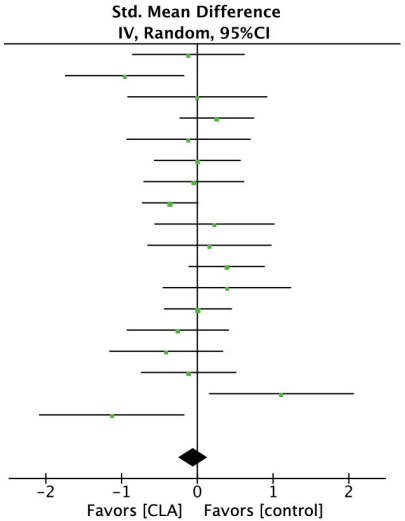
Xiamon S Gut Microbes 2024.

Fats

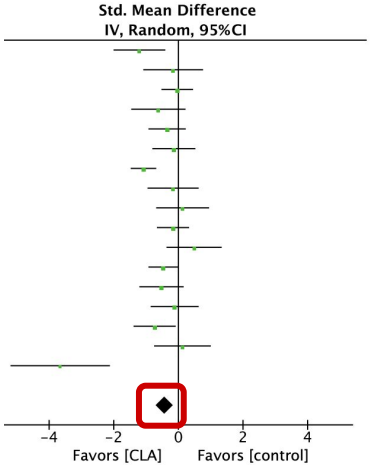



# **Conjugated Linoleic Acid** and Body Fat

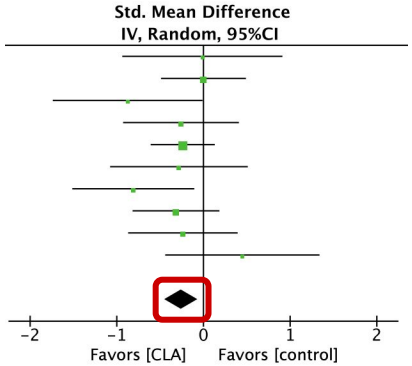
## Weight




## Body Fat




## Insulin Resistance



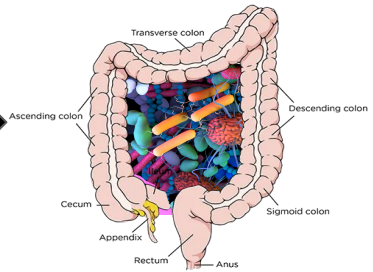

Liang CW. et al. Nutrition Review. 2023.

# Food-**Microbiome-Mitochondria**-Health Axis

## Microbiome
**Food Processor**

**Fiber**
**Phenols**

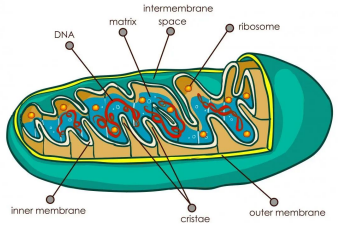
**Fats**




## Mitochondria
**Energy Powerhouse**

**SCFA's**
**Mod. Phenols**

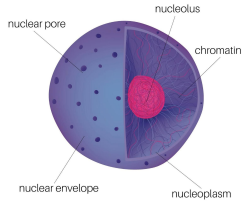
**Conj. Fats**




**ATP**
**NADH**

**Regulators**

## Nucleus
**Command Center**

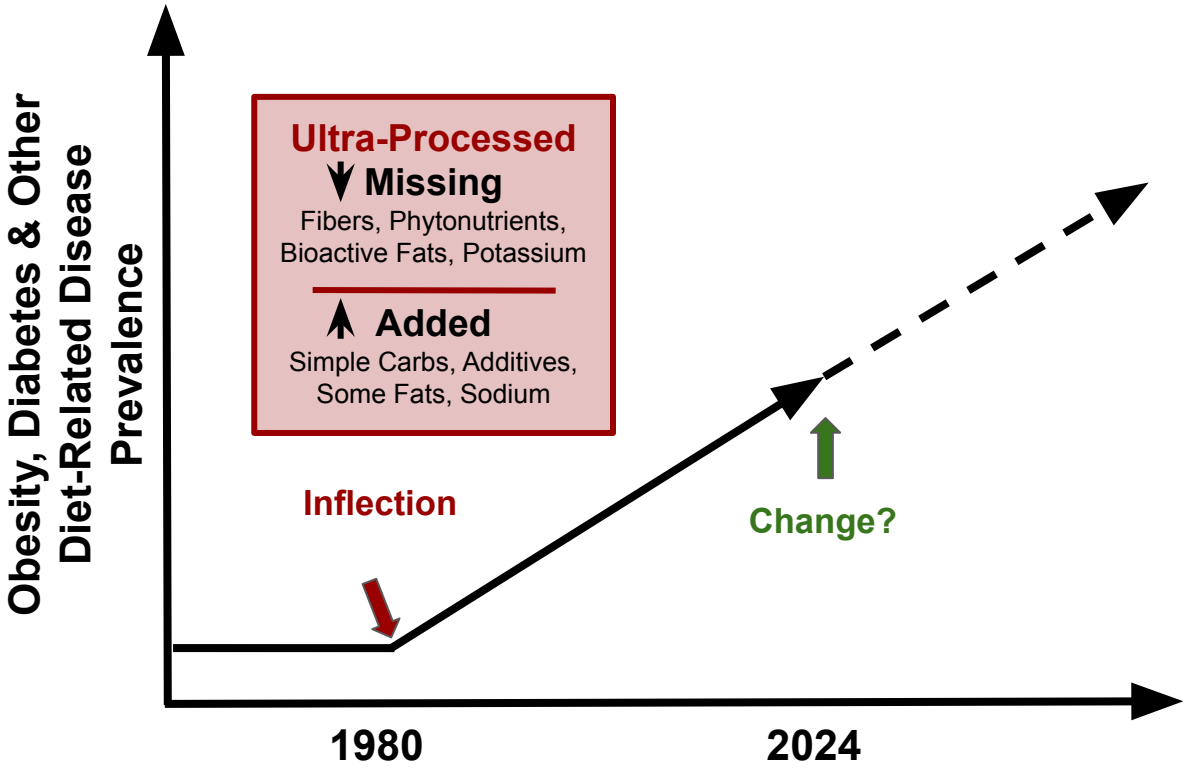



**Unhealthy Food→Depleted Microbiome → Dysfunctional Mitochondria → Disease**

| Metabolic Disease | Immune Disease | Frailty Disease | Neurologic Disease | Other Disease |
|---|---|---|---|---|
| • Obesity, Diabetes | • Autoimmune | • Osteopenia | • Alzheimer's | • Cardiovasc |
| • Stunting, Wasting | • Allergy | • Sarcopenia | • Mood | • Cancer |

Damman CJ. Advances in Nutrition 2023

# How To Effect Change?

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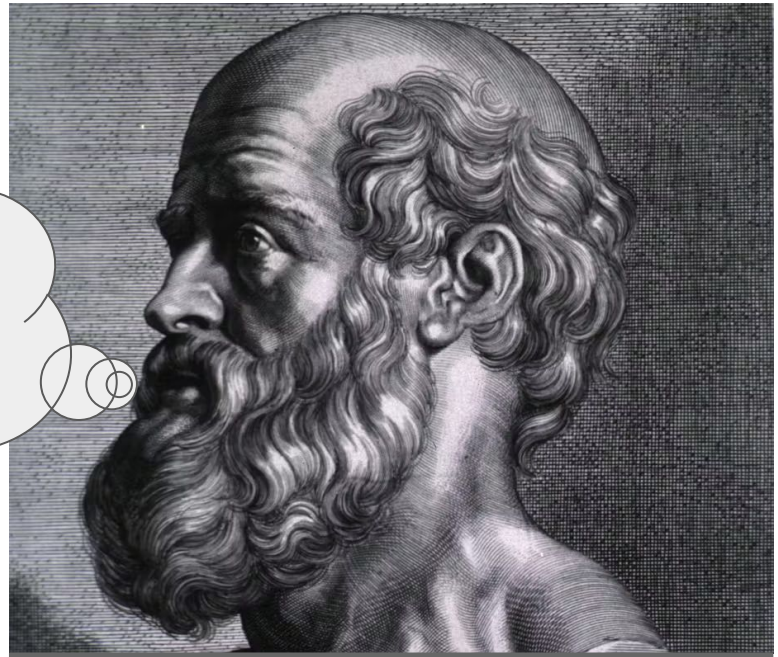
# “Let **Food…** Be Thy Medicine”-Hippocrates (400 BC)

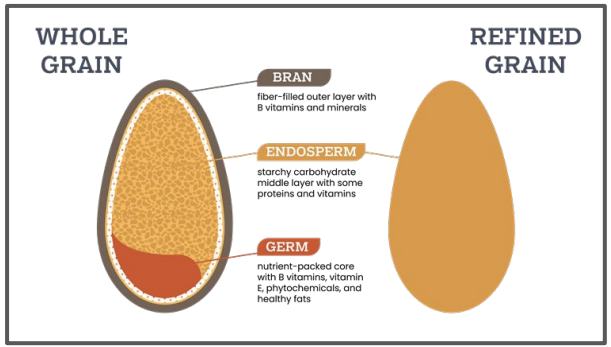
*…And It’s 4 F’s:*
*Fibers, Phenols, Fat*
*Bioactives & Ferments*



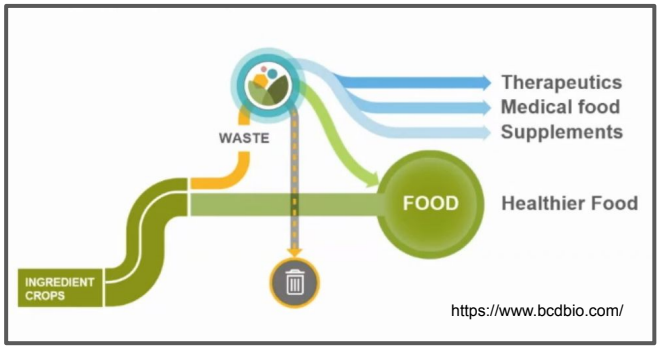
“Let Food Be Thy Medicine”
-Hippocrates (400 BC)

# Add Back What is Taken Out - Functional Nutrition

## Taken Out




## Foods that Add Back



# Dietary Solutions with Options

**Healthy Lifestyle Slog**

**Maximize Health**

**Comprehensive**

**Maximize Convenience**

**Magic Bullet Dream**

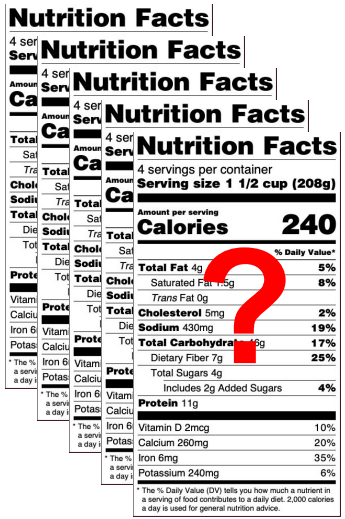
**Whole Food**

**Functional Nutrition**

**Supplement**

**Add back missing nutrients - fiber, phytonutrients, healthy fat - to maximize Health & Convenience?**

# A **Microbiome-Focused** Quality Score called NCS




## Algorithm

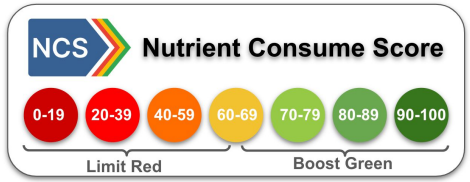
### Nutrient Ratios

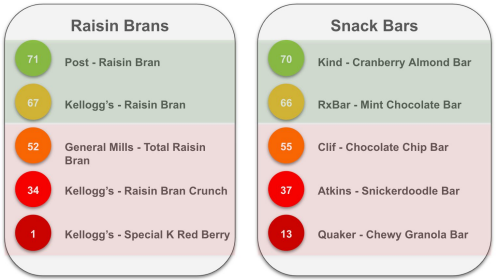
**Increased**

Fibers, Phytonutrients, Bioactive Fats, Potassium

**Decreased**

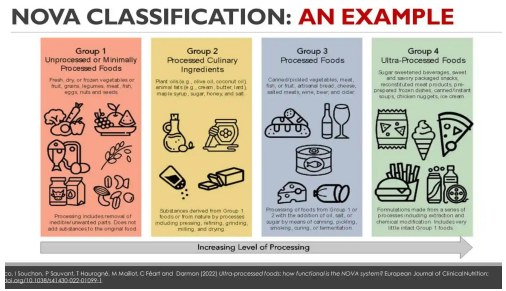
Simple Carbs, Additives, Saturated Fats, Sodium

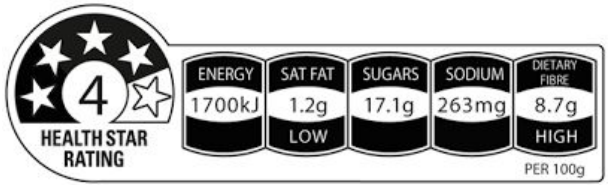


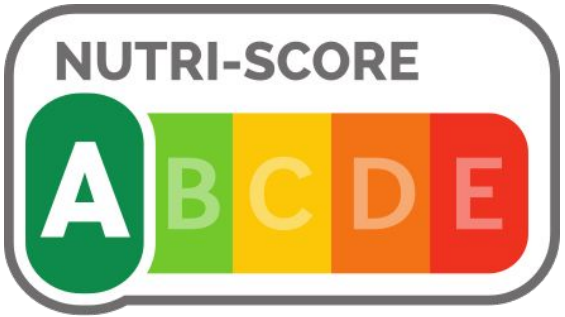




www.gutbites.org

# Other Available Nutrient Profile Systems (NPSs)

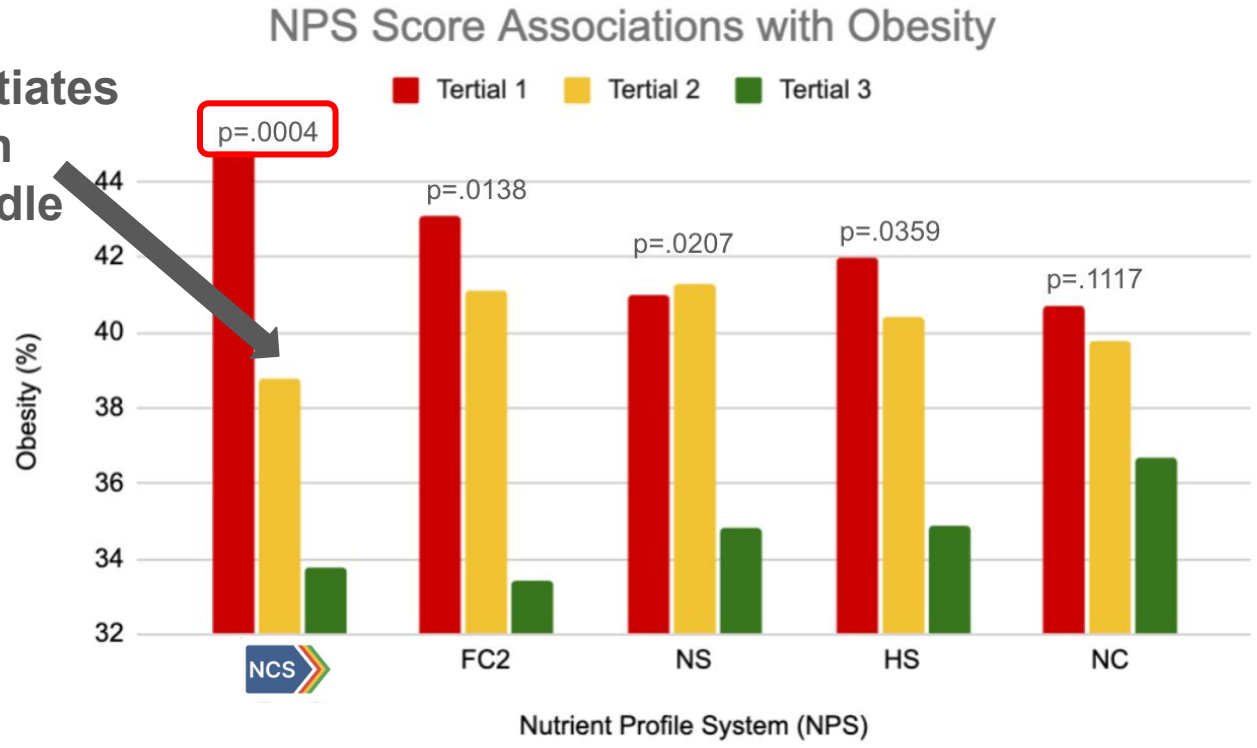


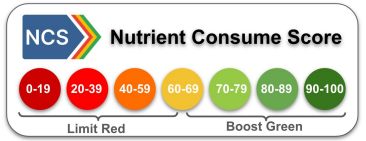




# Nutrient Consume Score Compared to ohters

**Differentiates Foods in The Middle**





Damman CJ. MedRxiv 2024.

# Theory of Change

## TECHNOLOGY

Whole Foods & Functional Foods


Informed Decisions

## CONSUMER PATH

Early Adoption

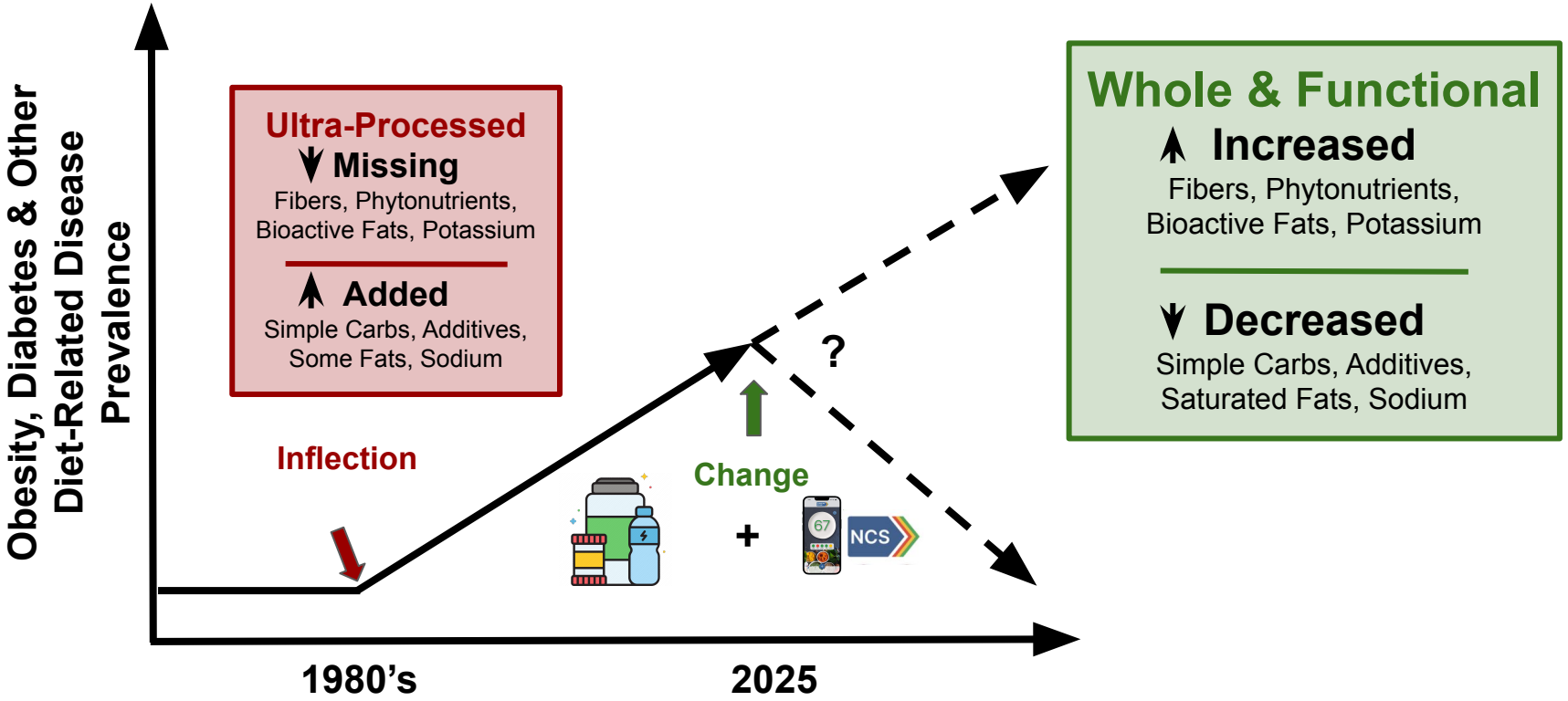
Big Food Changes

Public Adoption

## HEALTH

Disease Prevention

# Which Future?

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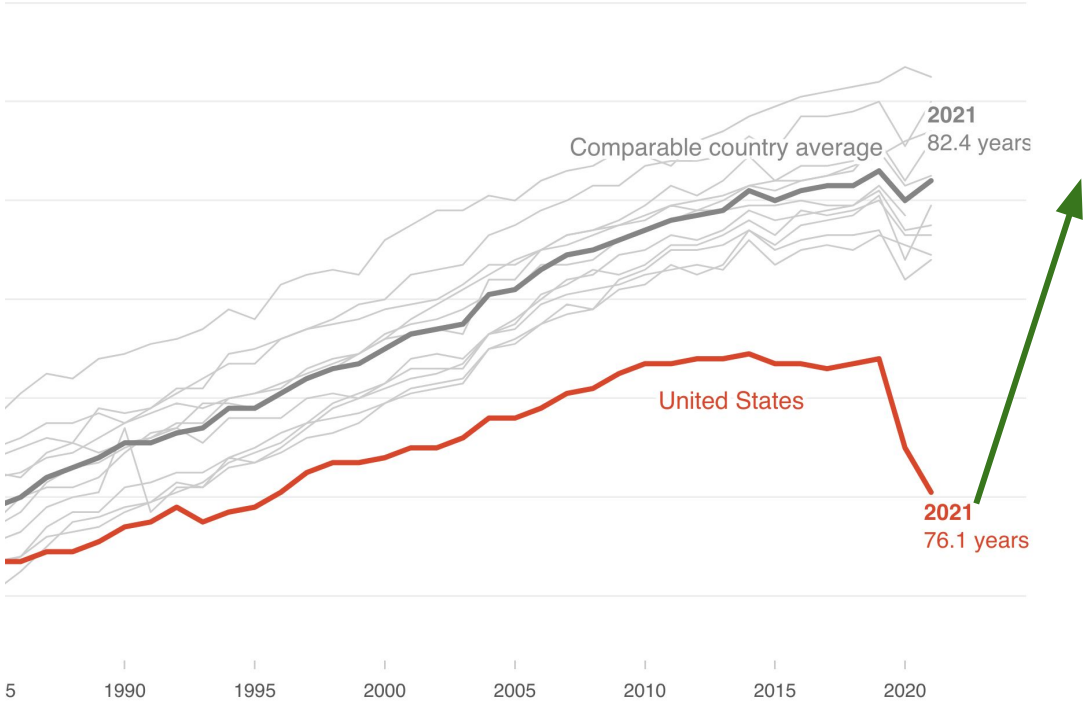
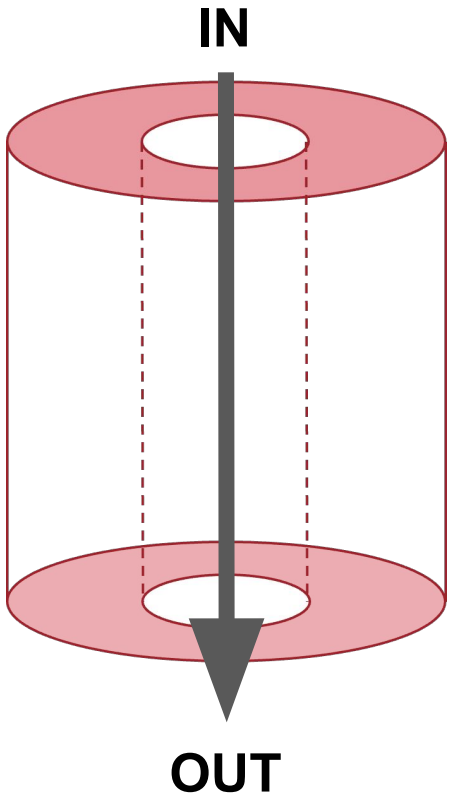
# United States Life Expectancy

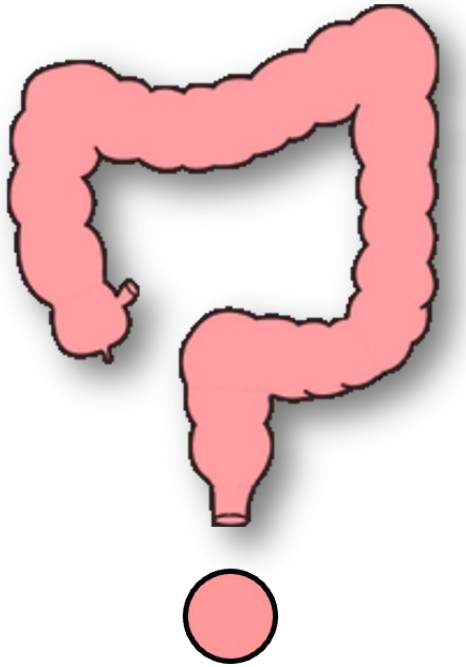



HealthSystemTracker.com

# What We Covered

- **Aging:**
  - US Life expectancy declining
  - Processed foods contributing
  - Microbiome is altered
- **Obesity/Metabolic Disease:**
  - Key contributor to unhealthy aging
  - Add back what is missing in food
  - Enable benefits of healthy microbiome
- **Future Solutions:**
  - Whole + Functional foods
  - Smart tech to informs choice





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