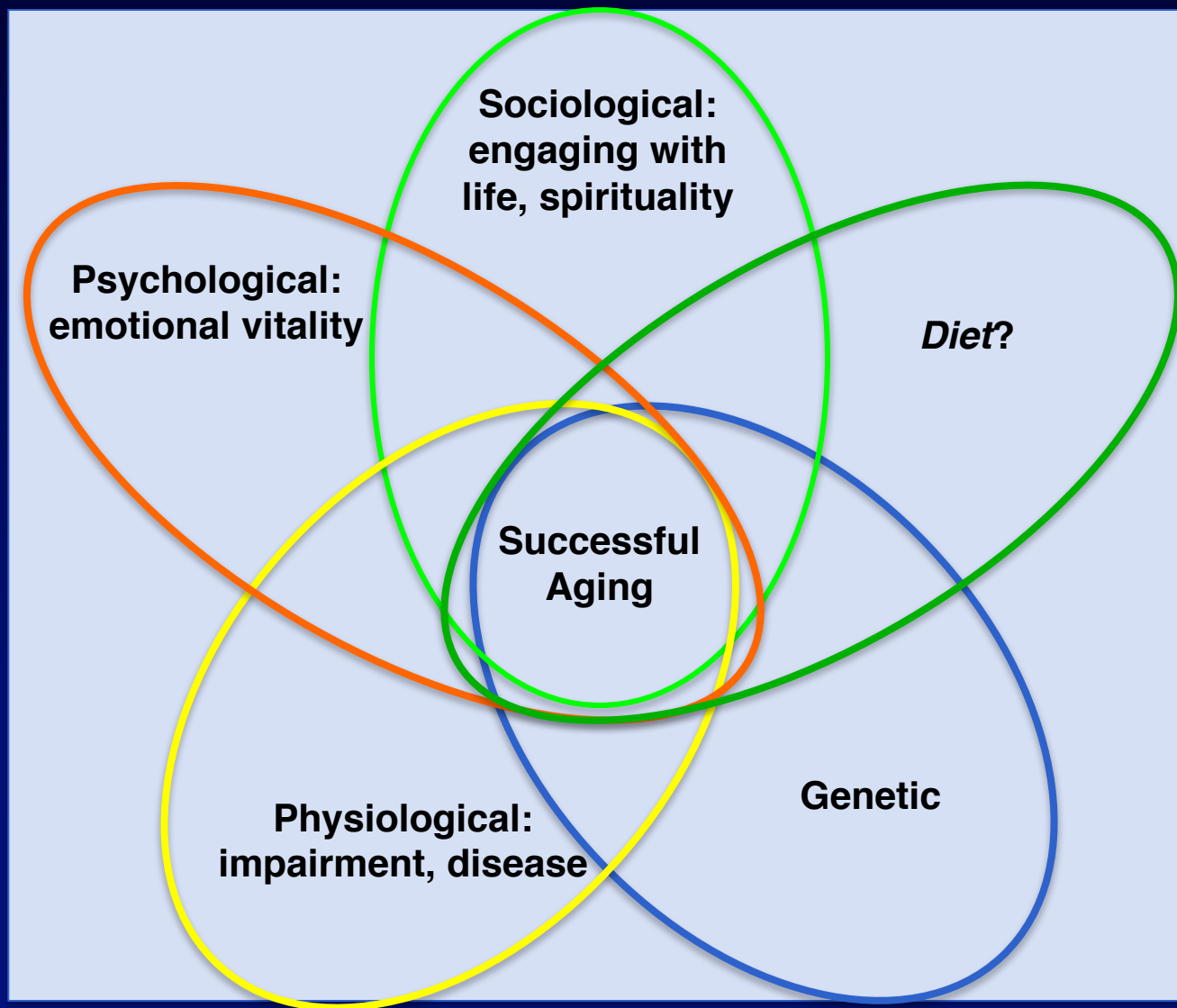


**International Alliance of Dietary and  
Food Supplement Associations  
16 May 2017 – Seoul, South Korea**

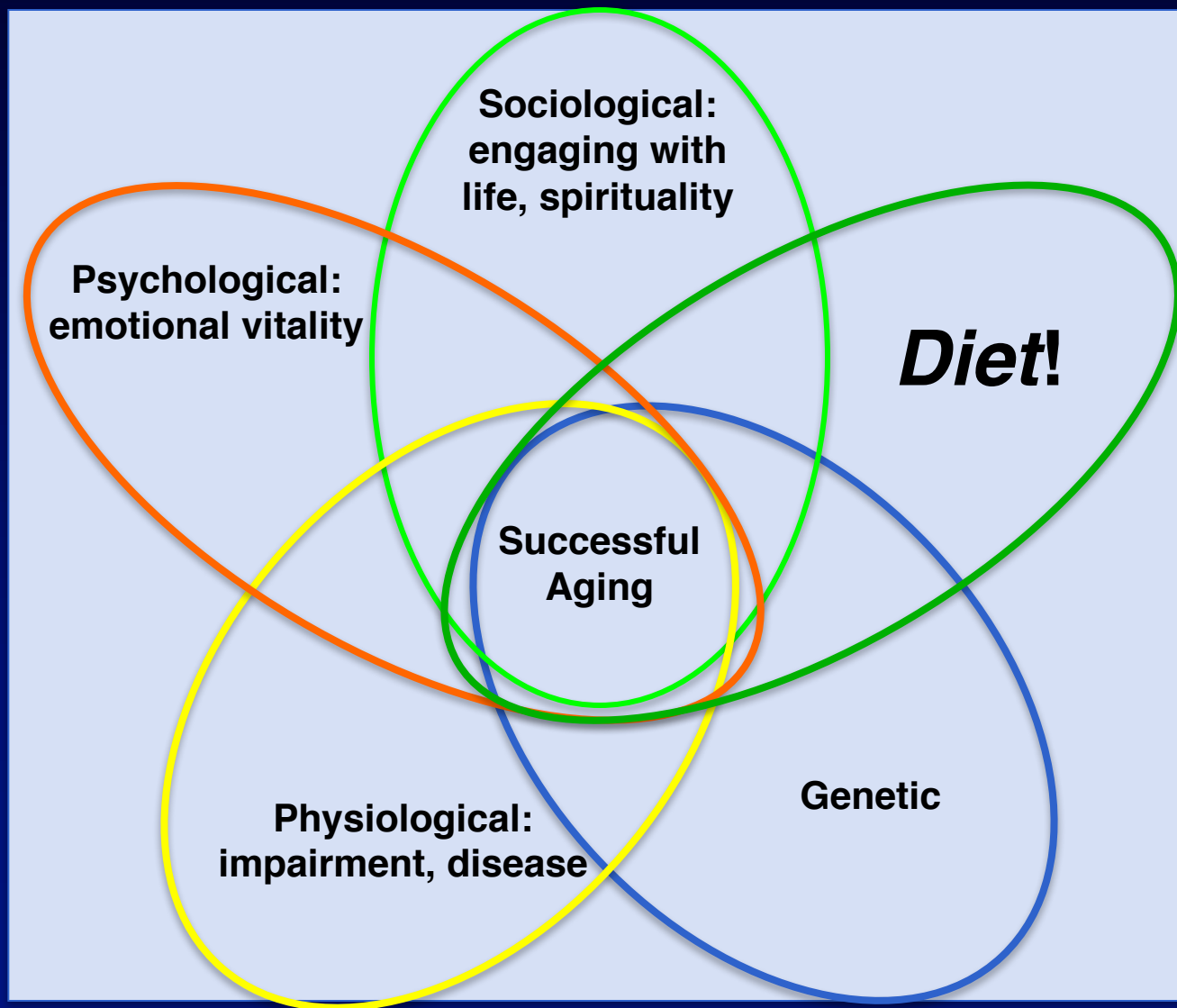
# **The Impact of Nutrition on Aspects of Healthy Aging**

**Jeffrey Blumberg, PhD, FASN, FACN, CNS-S  
Friedman School of Nutrition Science and Policy  
Jean Mayer USDA Human Nutrition Research Center on Aging  
Tufts University  
Boston, MA USA**

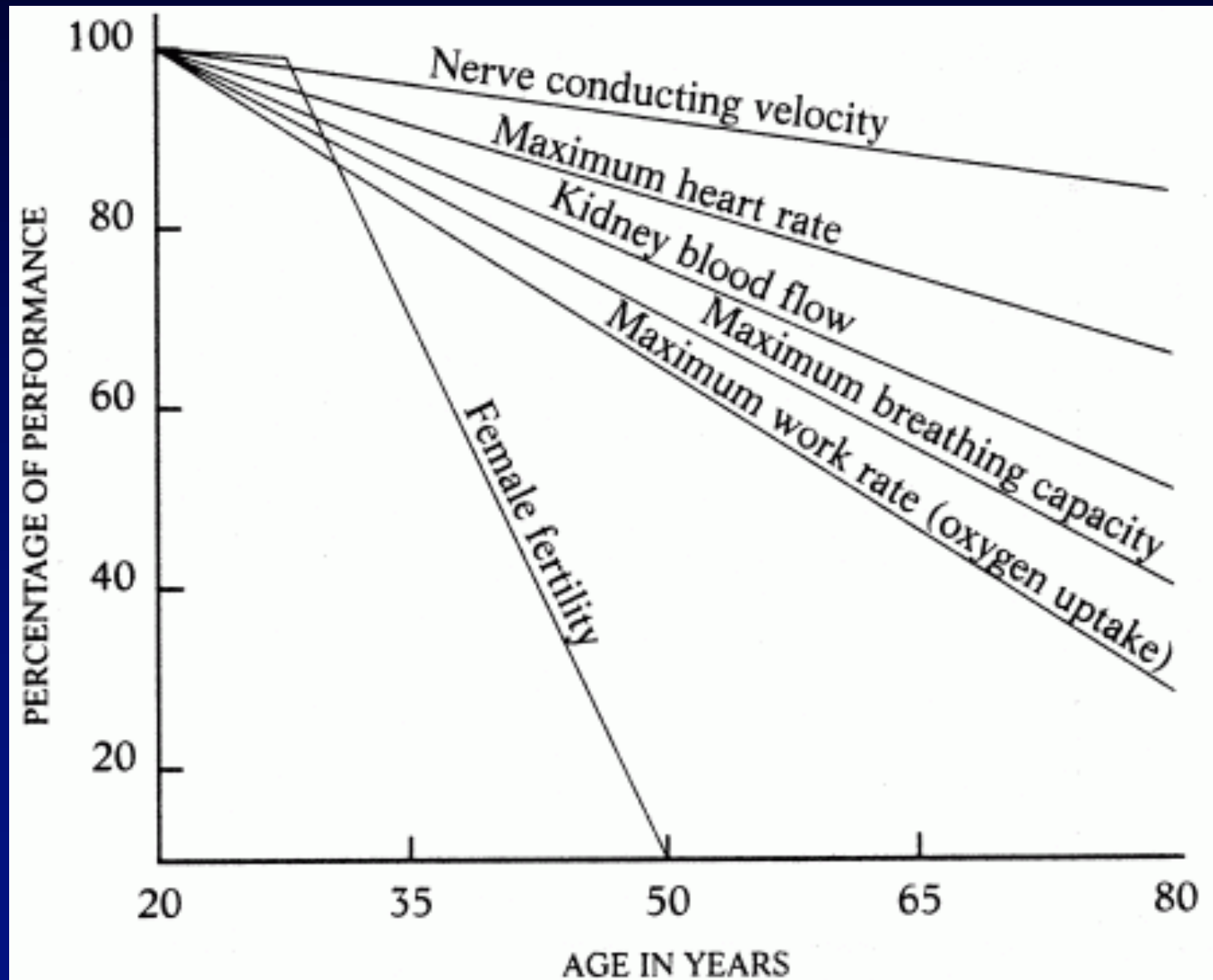
# Successful Aging



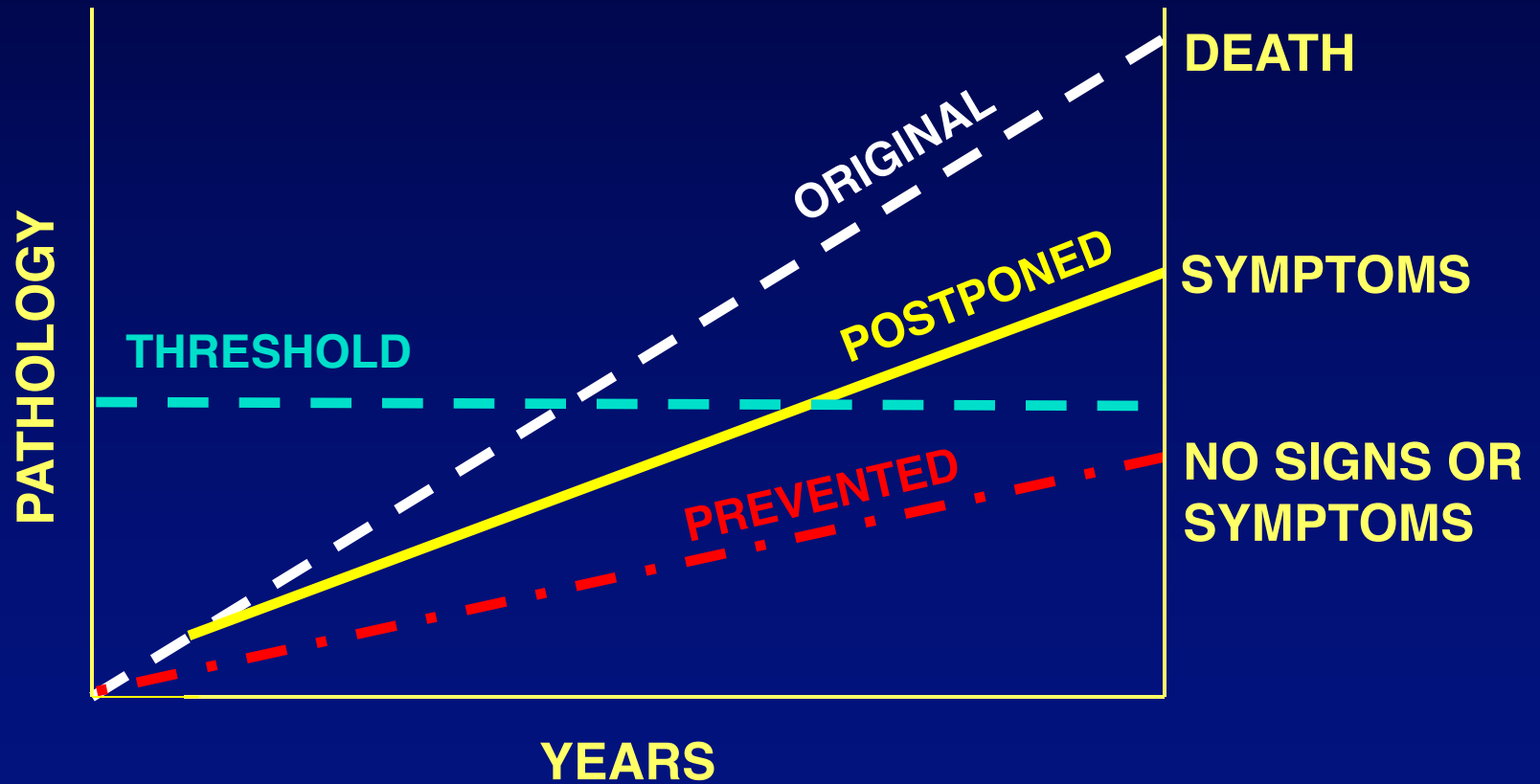
# Successful Aging



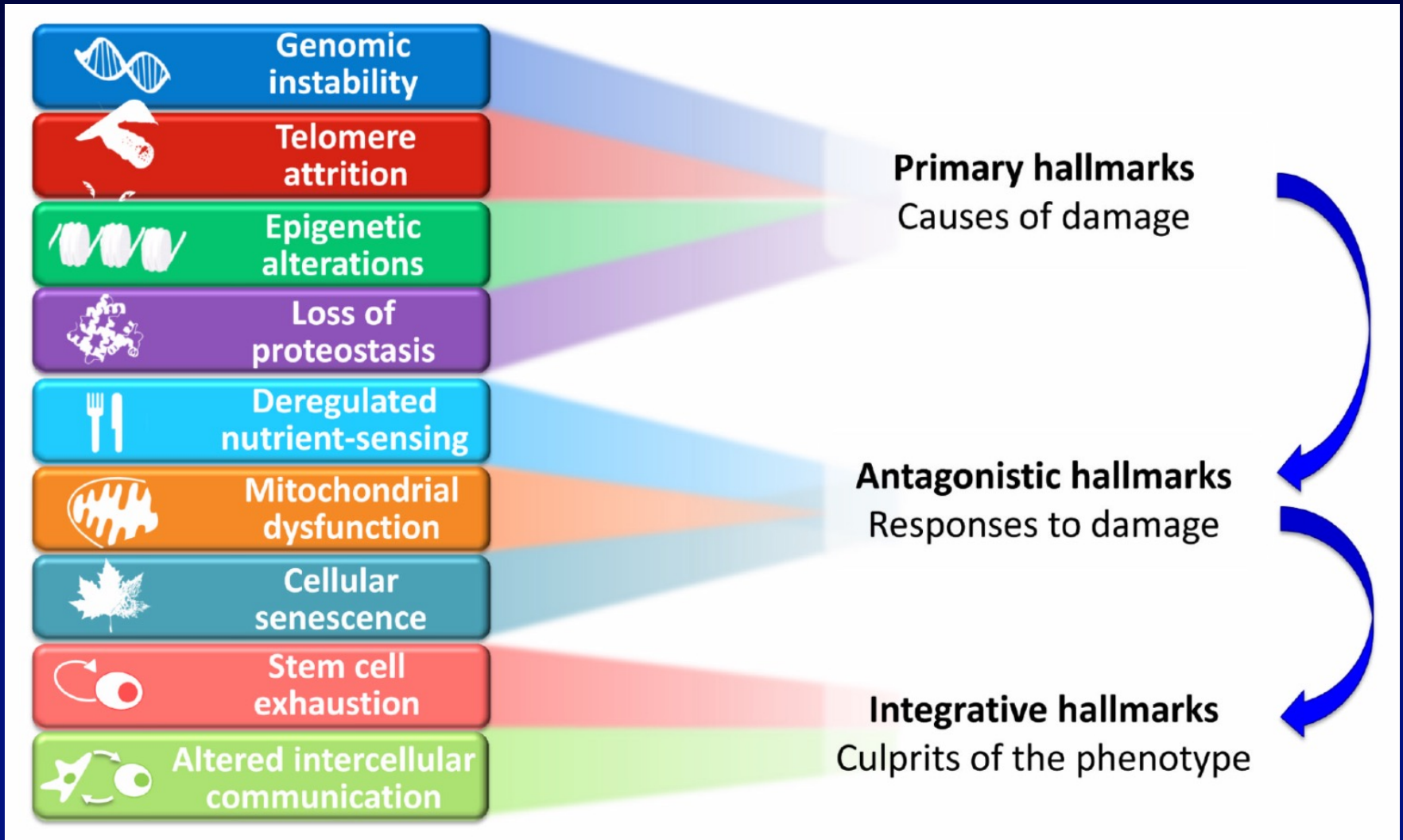
# Age-related Declines in Physiological Function



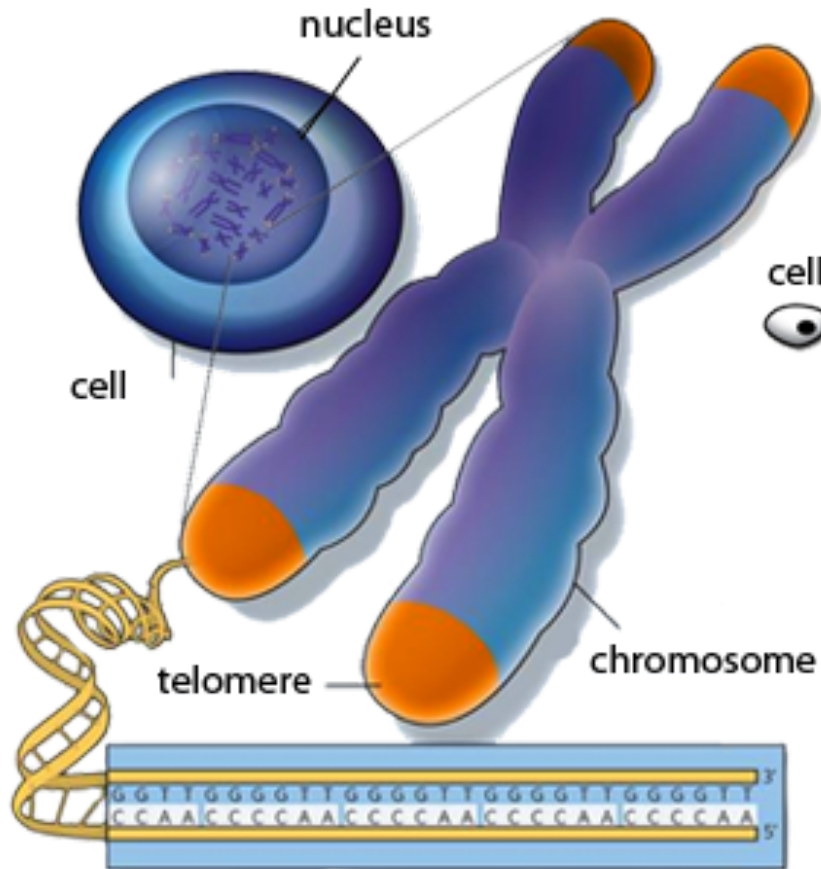
# Preventive Nutrition and Aging



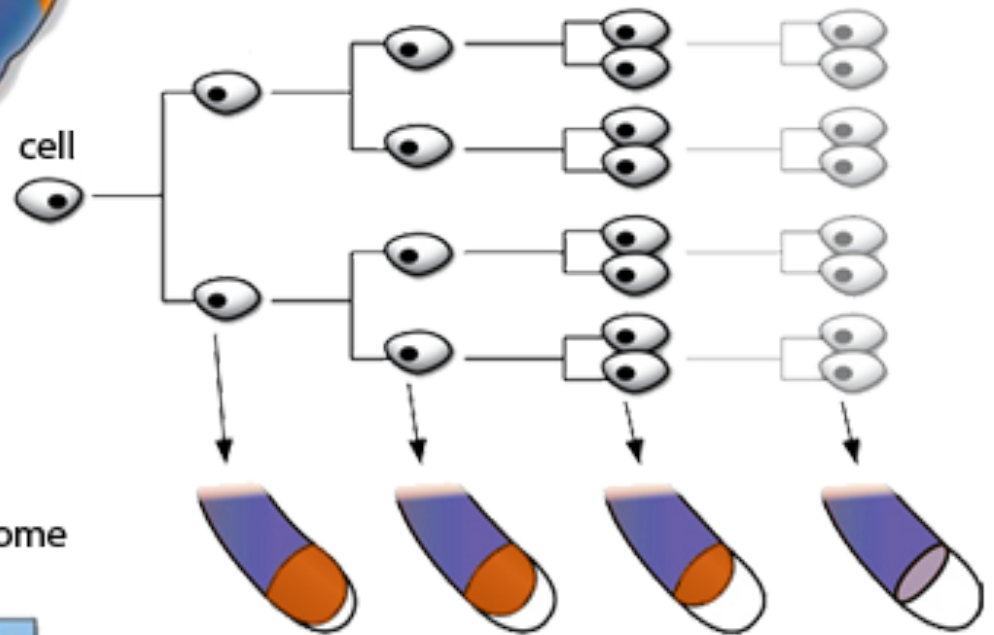
# Functional Interconnections Between Hallmarks of Aging



# Telomere Attrition

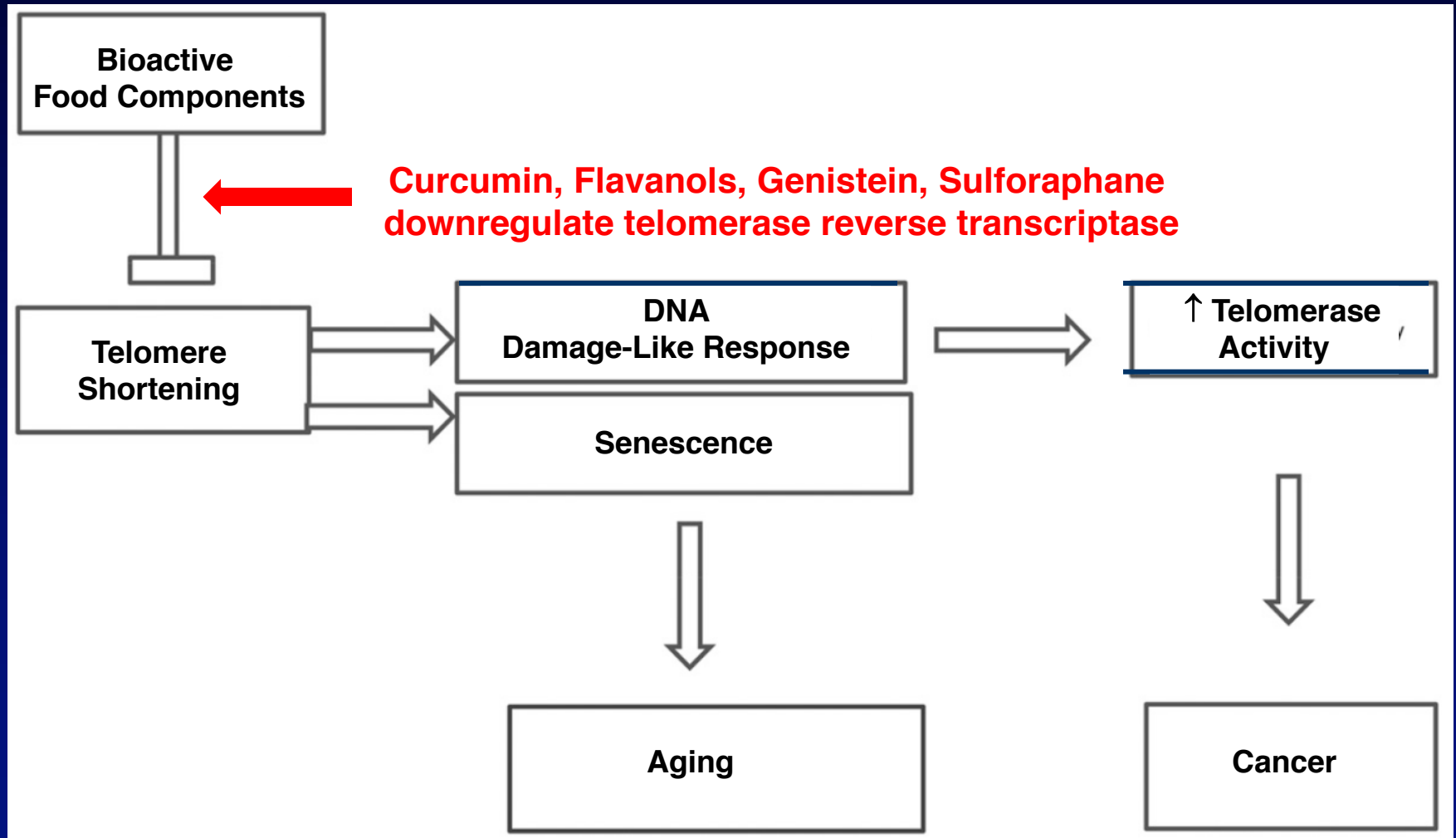


*As the cell divide overtime (healthy cell)...*



*...telomeres shorten until  
cell division stops (senescence).*

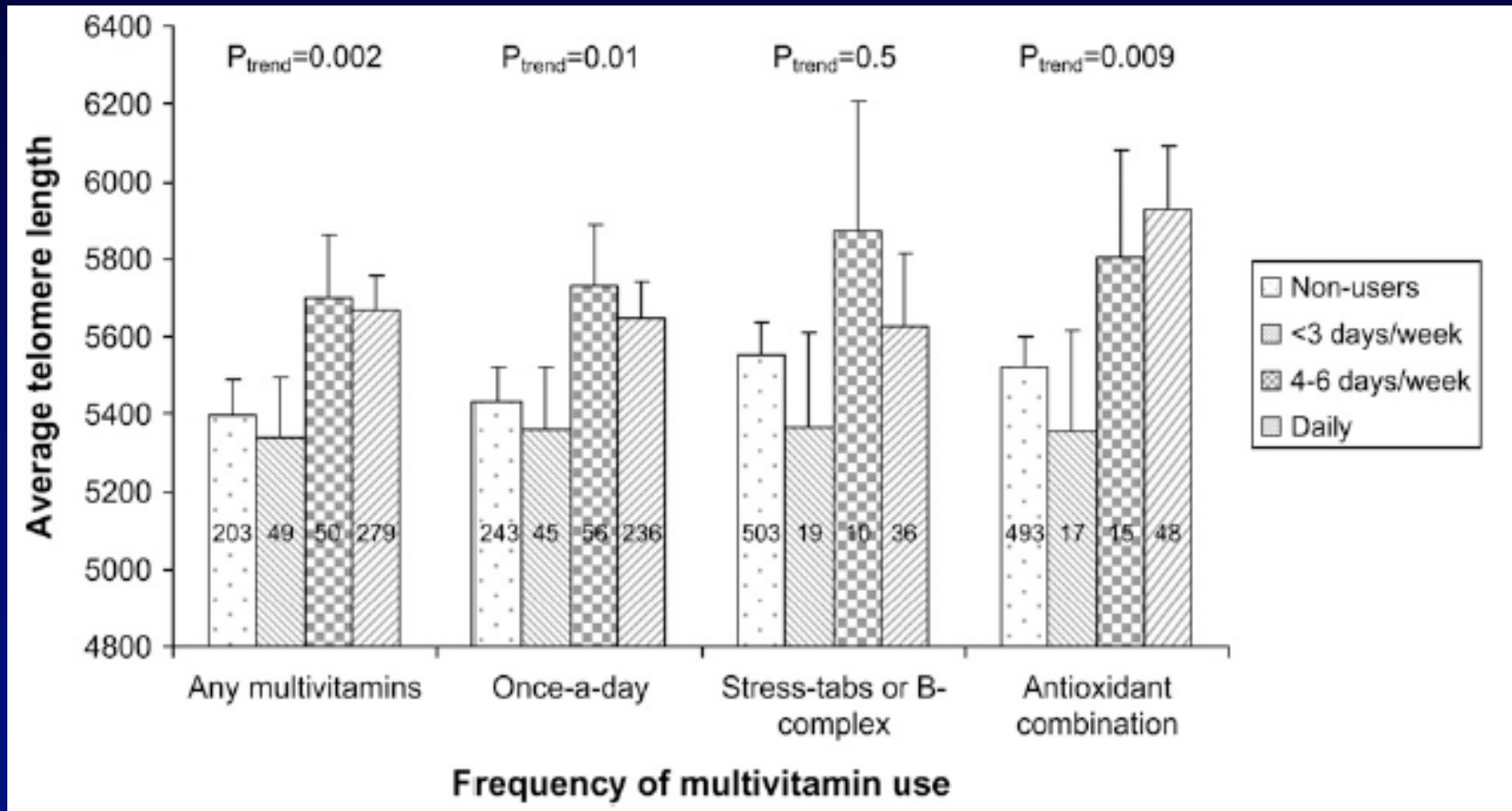
# Telomerase as a Target for Phytochemicals





# Multivitamin Use is Positively Associated with Telomere Length in Women

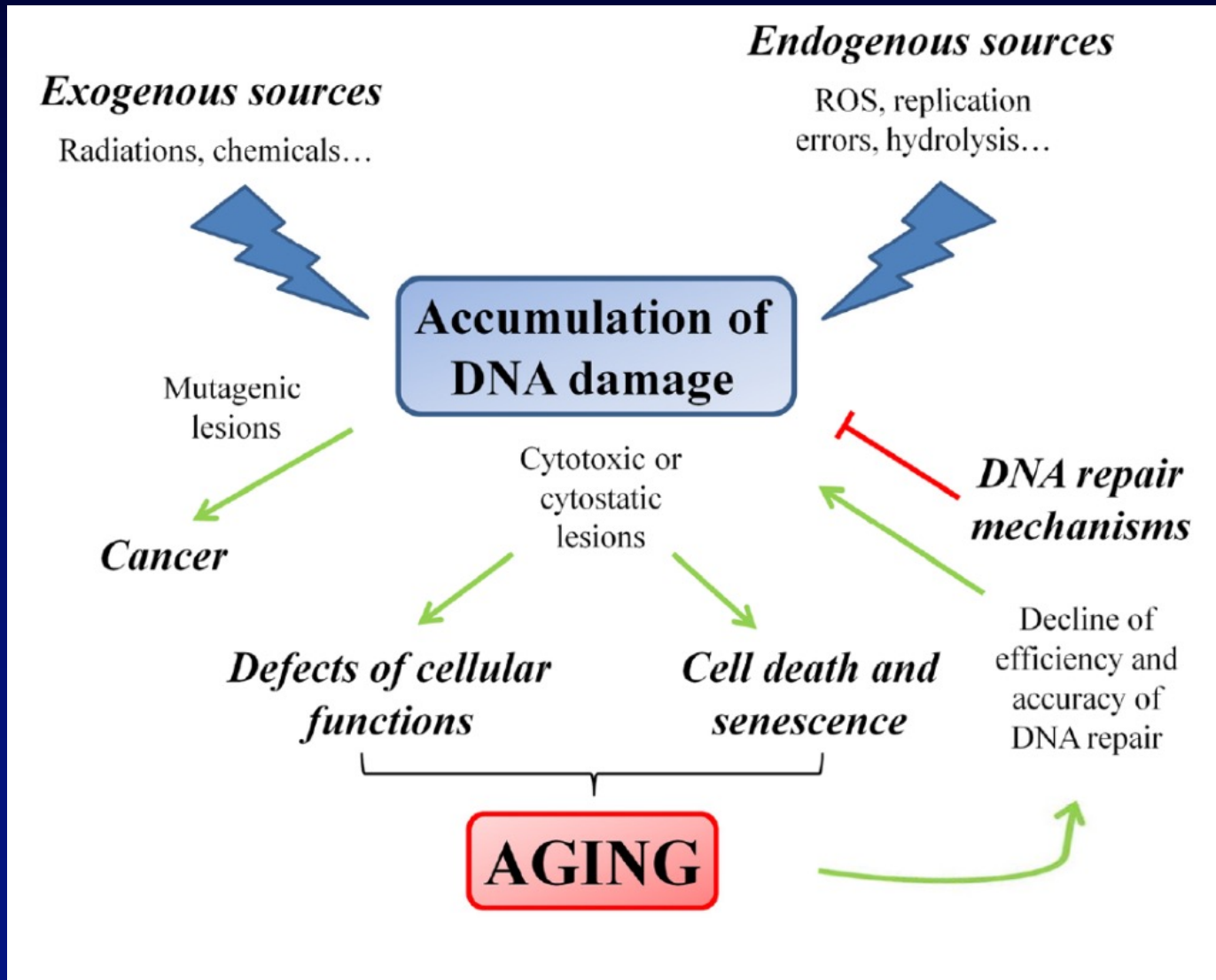
## *Sister Study*



**Cohort XS**

- n, 586
- age, 35-74











# DNA Damage Response and Aging



# β-Carotene, Lutein, and/or Lycopene Protect Against DNA Damage

## RCT

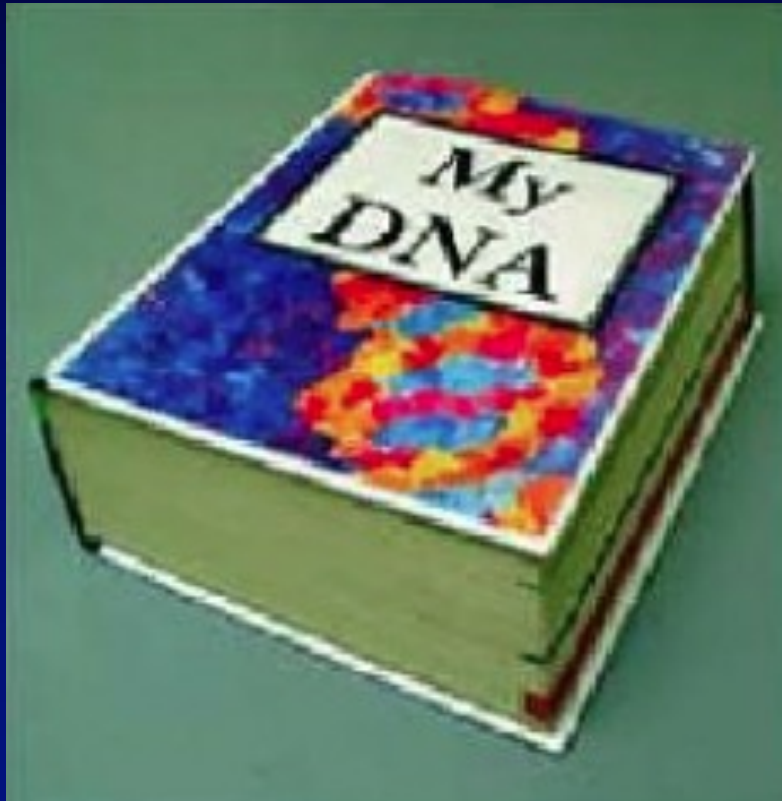
- n, 37 women
- age, 50-70 y
- duration, 56 d
- dose, 12 mg/d

| Scores                     | 0   | 1   | 2   | 3   | 4   |
|----------------------------|---|---|---|---|---|
| Percentage DNA in the tail | <5  | 5-20  | 20-40   | 40-80   | >80   |
| Average                    | 2.5   | 12.5  | 30  | 60  | 90  |
|                            |  |  |  |  |  |
|                            | 0%  | 6.8%  | 25%   | 55%   | 85%   |
|                            |  |  |  |  |  |
|                            | 0%  | 12%   | 28%   | 65%   | 97%   |

| Group   | Day 1                   | Day 15                 | Day 29                 | Day 43                 | Day 57                 |
|---|-------------------------|------------------------|------------------------|------------------------|------------------------|
| Endogenous DNA damage (%) <sup>2</sup>                |                         |                        |                        |                        |                        |
| Placebo (n = 6)                                       | 8.7 ± 0.8               | 9.0 ± 1.0              | 10.6 ± 1.3             | 9.2 ± 1.7              | 9.9 ± 1.5              |
| Mixed carotenoids (n = 8)                             | 10.9 ± 0.6              | 8.6 ± 0.6 <sup>3</sup> | 7.9 ± 0.7 <sup>3</sup> | 7.1 ± 0.5 <sup>3</sup> | 7.0 ± 0.4 <sup>3</sup> |
| Lutein (n = 8)  | 10.6 ± 0.5              | 9.4 ± 0.7              | 9.5 ± 0.5              | 7.7 ± 0.5 <sup>3</sup> | 7.1 ± 0.6 <sup>3</sup> |
| β-Carotene (n = 7)                                    | 12.4 ± 1.0 <sup>4</sup> | 9.7 ± 0.9 <sup>5</sup> | 8.6 ± 1.1 <sup>3</sup> | 9.4 ± 0.9 <sup>3</sup> | 8.0 ± 0.7 <sup>3</sup> |
| Lycopene (n = 8)                                      | 11.9 ± 0.9              | 10.0 ± 1.2             | 9.0 ± 0.9 <sup>3</sup> | 7.5 ± 0.7 <sup>3</sup> | 6.8 ± 0.6 <sup>3</sup> |
| Hydrogen peroxide-induced DNA damage (%) <sup>6</sup> |                         |                        |                        |                        |                        |
| Placebo (n = 6)                                       | 42.1 ± 2.2              | 44.6 ± 2.4             | 39.7 ± 1.1             | 43.0 ± 2.9             | 40.6 ± 3.1             |
| Mixed carotenoids (n = 8)                             | 44.2 ± 2.5              | 43.2 ± 3.3             | 42.6 ± 2.9             | 37.1 ± 4.0             | 36.4 ± 2.2             |
| Lutein (n = 8)  | 42.8 ± 2.4              | 43.5 ± 2.2             | 43.1 ± 2.0             | 41.5 ± 3.3             | 39.8 ± 3.0             |
| β-Carotene (n = 7)                                    | 48.2 ± 2.3              | 44.5 ± 3.4             | 41.1 ± 2.4             | 44.2 ± 2.1             | 38.0 ± 1.8             |
| Lycopene (n = 8)                                      | 50.5 ± 3.2              | 49.2 ± 3.6             | 51.1 ± 1.2             | 50.0 ± 2.3             | 42.5 ± 2.3             |

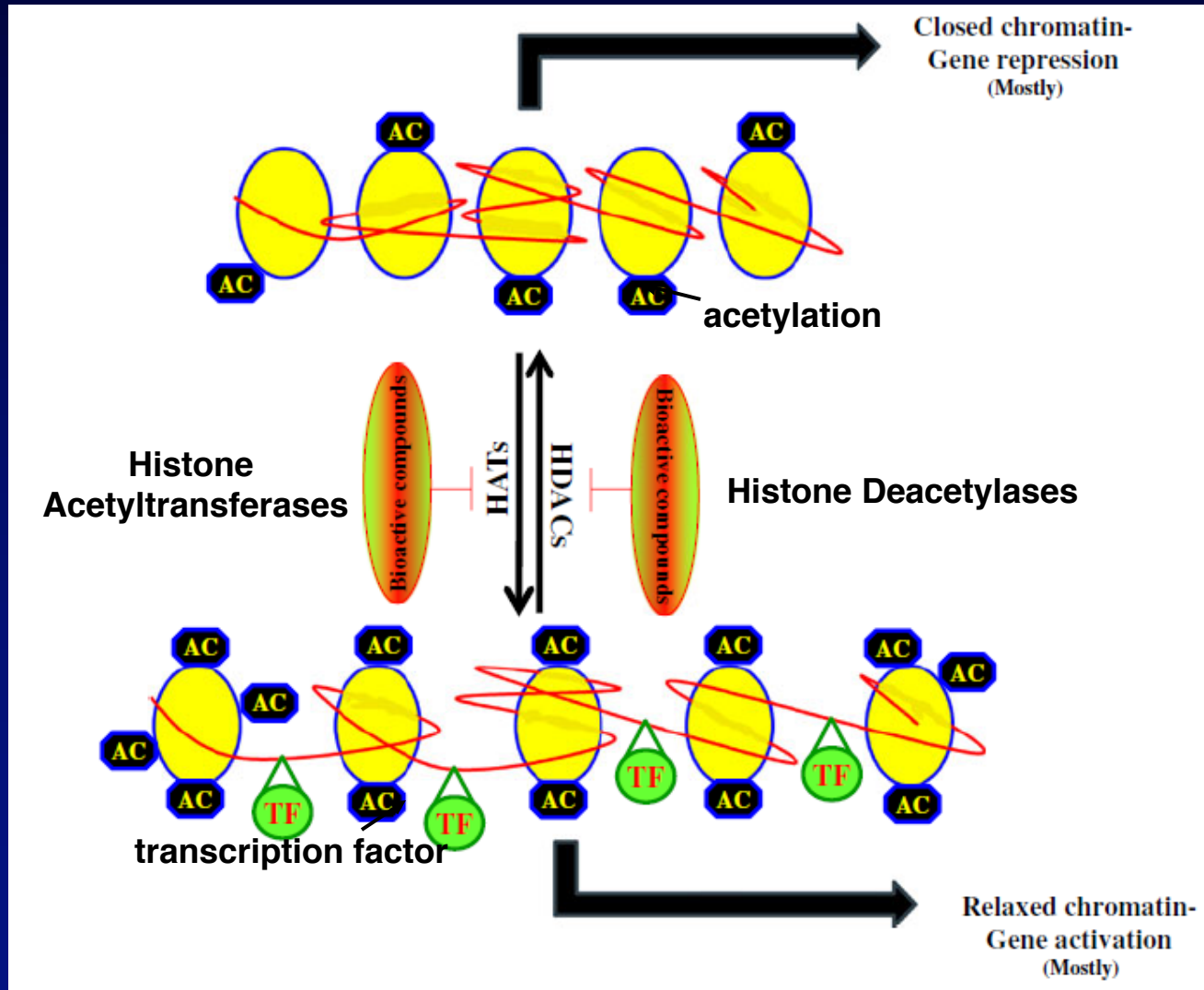
# DNA Damage: Genetics vs. Epigenetics

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# HATs Relax Chromatin → Gene Activation

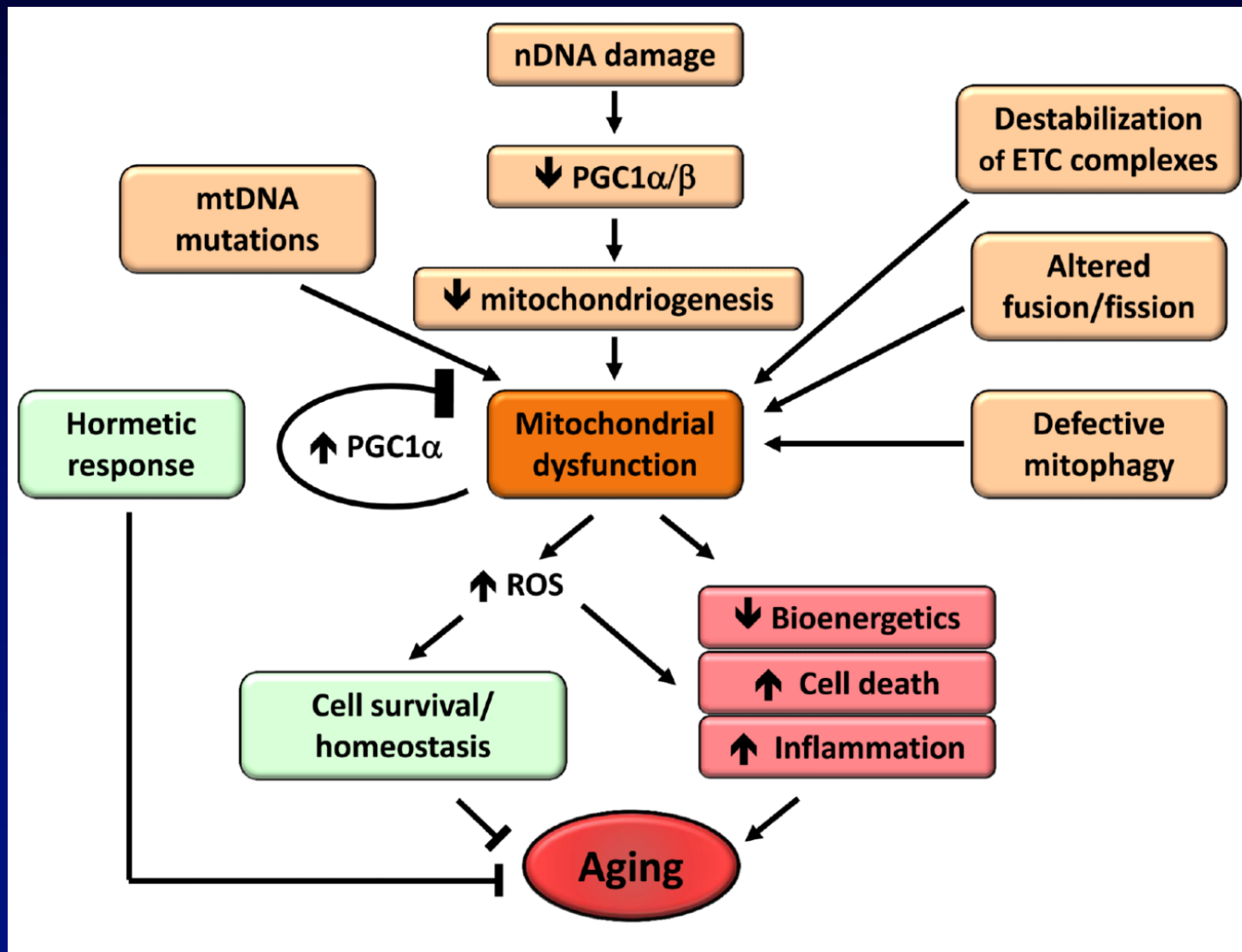
## HDACs Close Chromatin → Gene Repression



# Epigenetic Targets of Phytochemicals

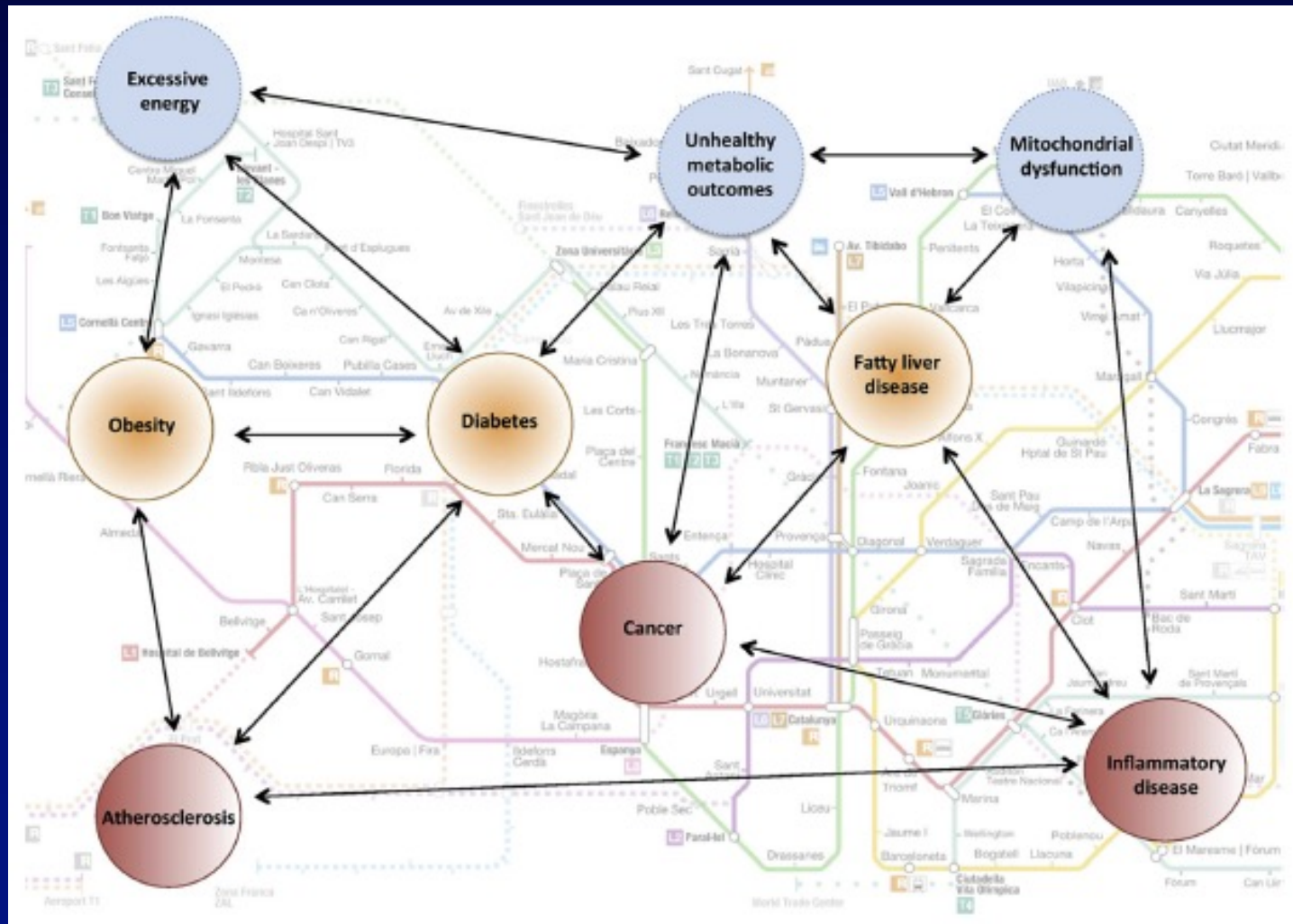
| <i>Dietary Bioactive</i> |   | <i>Epigenetic Target</i> |
|--------------------------|---|--------------------------|
| Apigenin                 |    | ↓ DNMT                   |
| Allyl mecaptan           |    | ↓ HDAC                   |
| Curcumin                 |    | ↓ DNMT, HDAC, HAT        |
| EGCG                     |    | ↓ DNMT, HAT              |
| Genistein                |    | ↓ DNMT, HDAC ↑ HAT       |
| Resveratrol              |    | ↓ DNMT    ↑ SIRT1        |
| Silymarin                |   | ↑ SIRT1                  |
| Sulforaphane             |  | ↓ DNMT, HDAC             |

# Mitochondrial Dysfunction as a Target for Aging





# Dynamic Network Links Cellular Pathways of Inflammation and Mitochondrial Function to Food and Nutrients

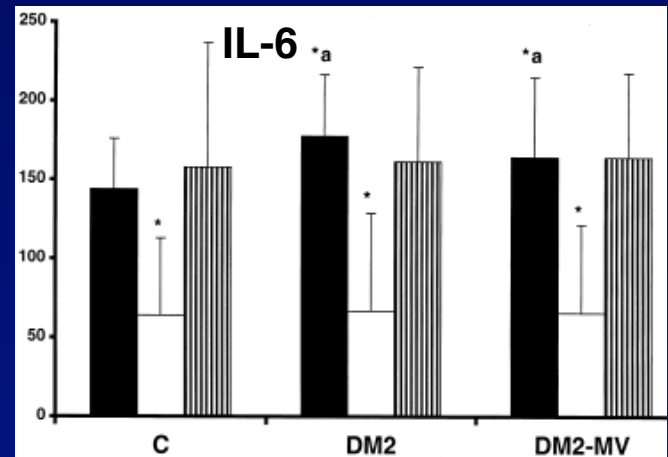
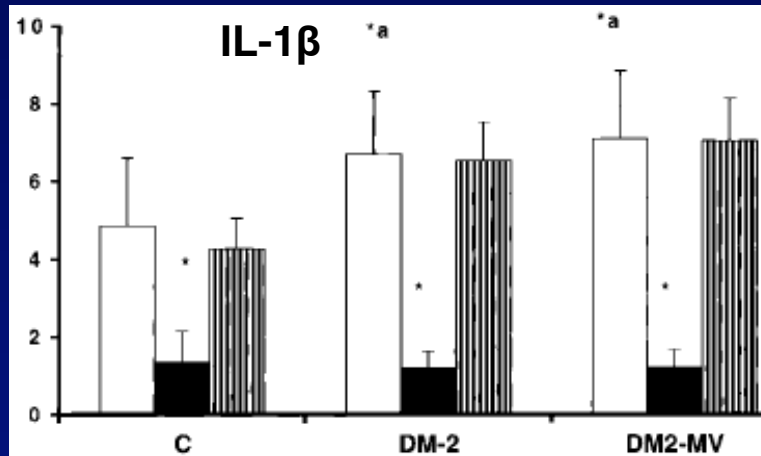
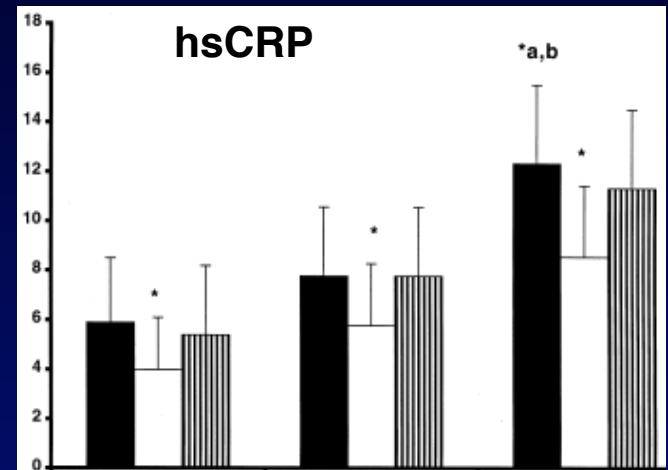
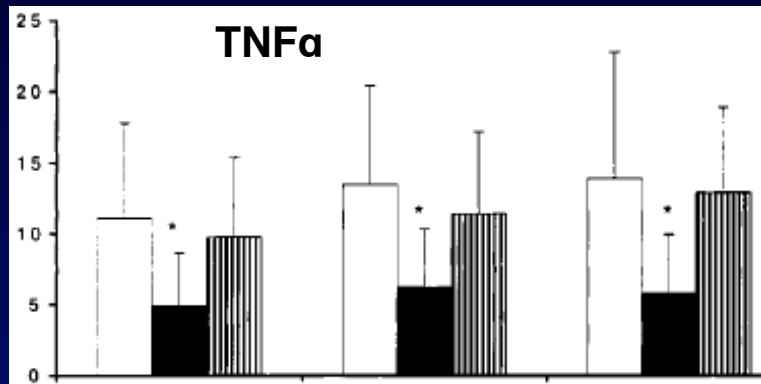




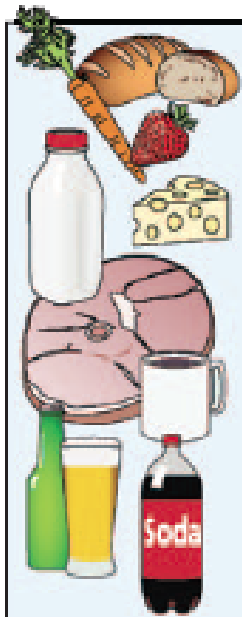
# Anti-inflammatory Actions of Vitamin E

## RCT

- n, 75
- age, 57 y
- F/U, 3 mo
- dose, 1200 IU/d



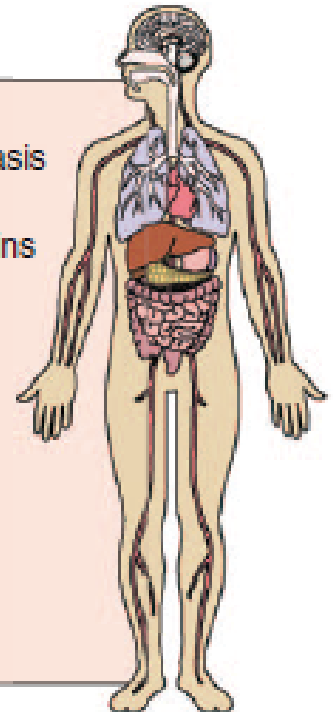
# Supoptimal Dietary Patterns are a Leading Cause of Poor Health



Refined grains, starches, sugars  
Fruits, vegetables, nuts  
Whole grains, legumes  
Yogurt, cheese, milk  
Fish, shellfish  
Processed meats, red meats  
Vegetable oils, specific fatty acids  
Coffee, tea, alcohol  
Sugary beverages, juice  
Minerals, antioxidants, phytochemicals  
Food-based dietary patterns  
Food processing, preparation methods

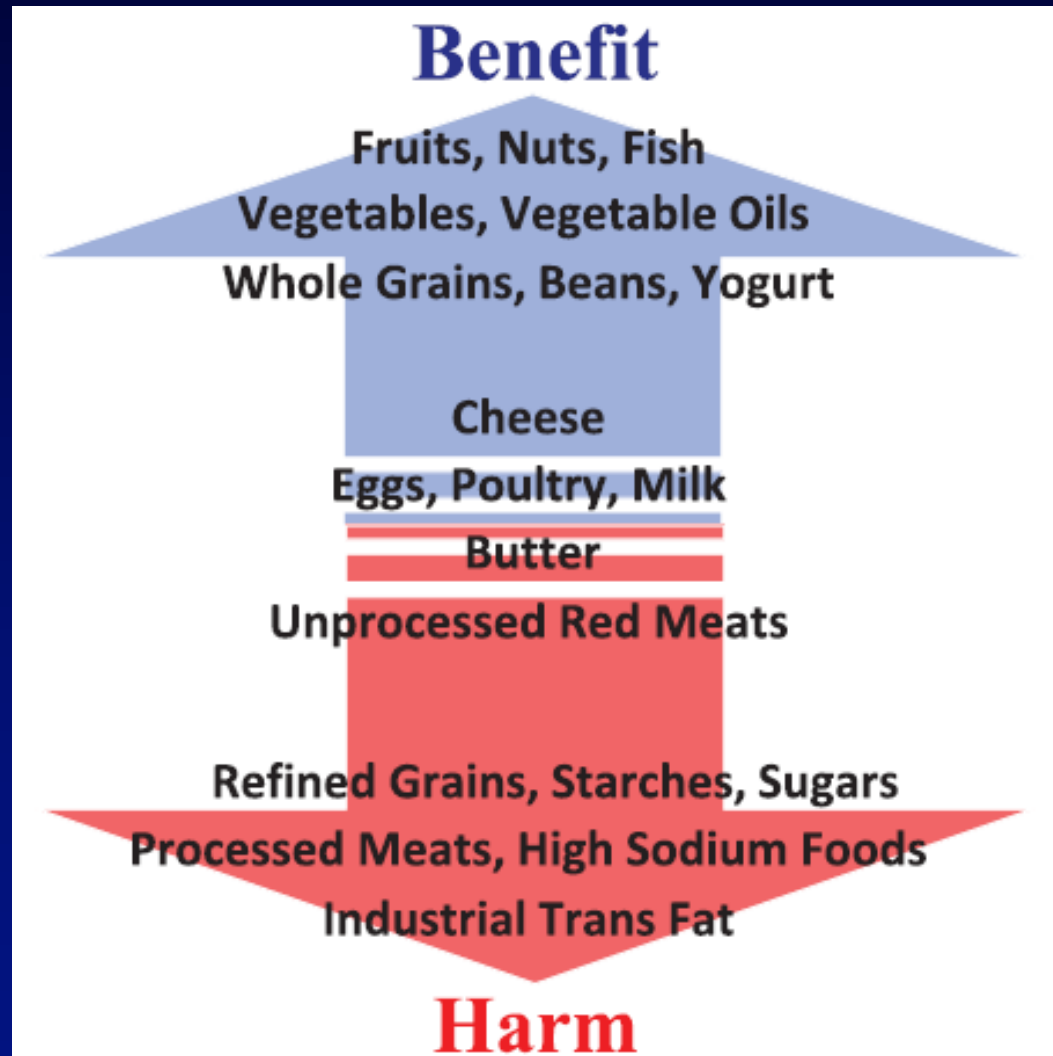


Blood pressure  
Glucose-insulin homeostasis  
Liver fat synthesis  
Blood lipids, apolipoproteins  
Endothelial function  
Systemic inflammation  
Brain reward, craving  
Gut microbiome  
Satiety, hunger, obesity  
Adipocyte function  
Cardiac function  
Thrombosis, coagulation  
Vasular adhesion



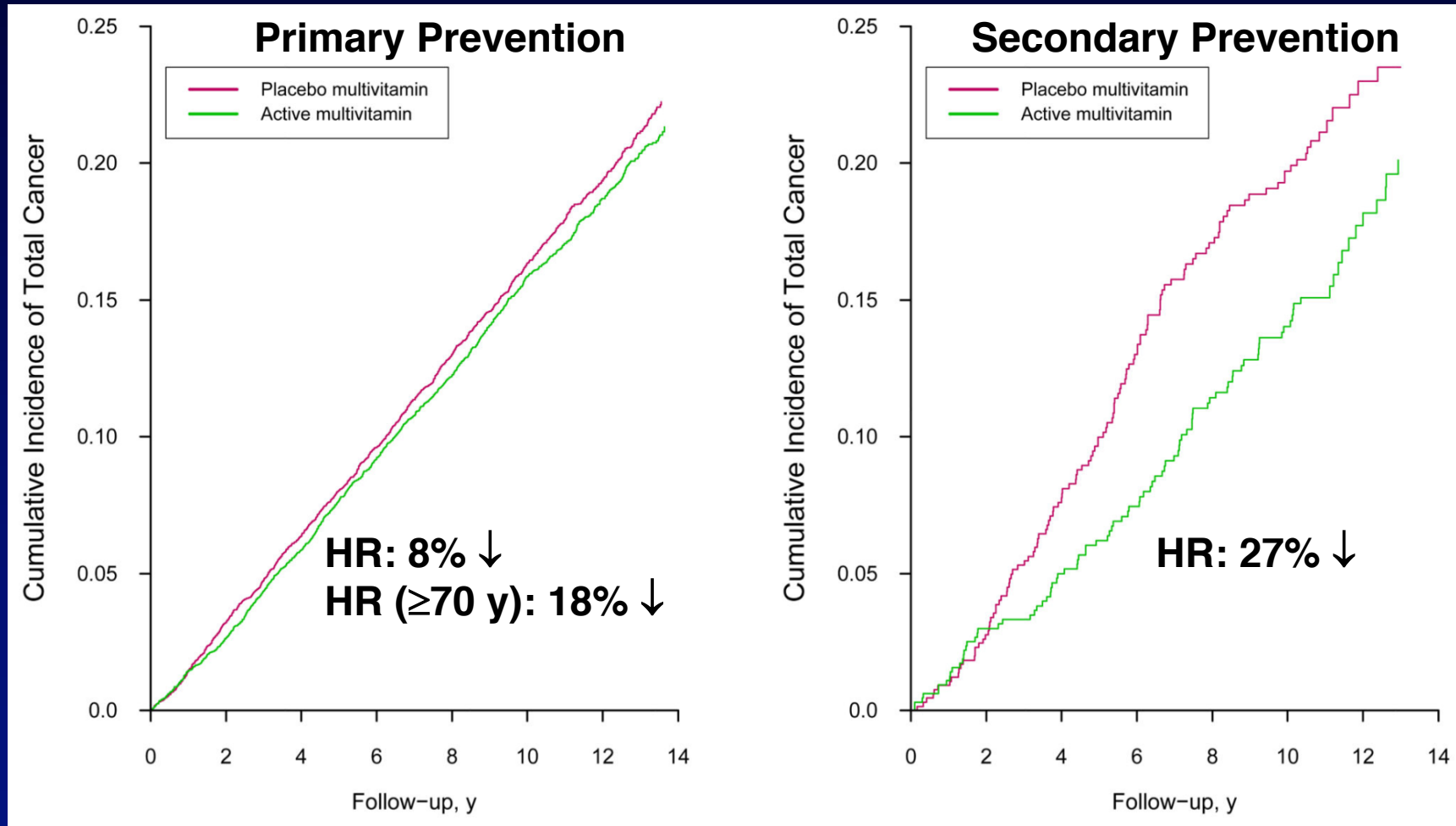
# Evidence-based Dietary Priorities for Cardiometabolic Health

---



# Multivitamins Reduce the Risk of Total Cancer

## *Physicians' Health Study II*



**RCT** • n, 14,641 men  
• age, ≥50 y

# Antioxidants Slow Progression to Age-Related Macular Degeneration

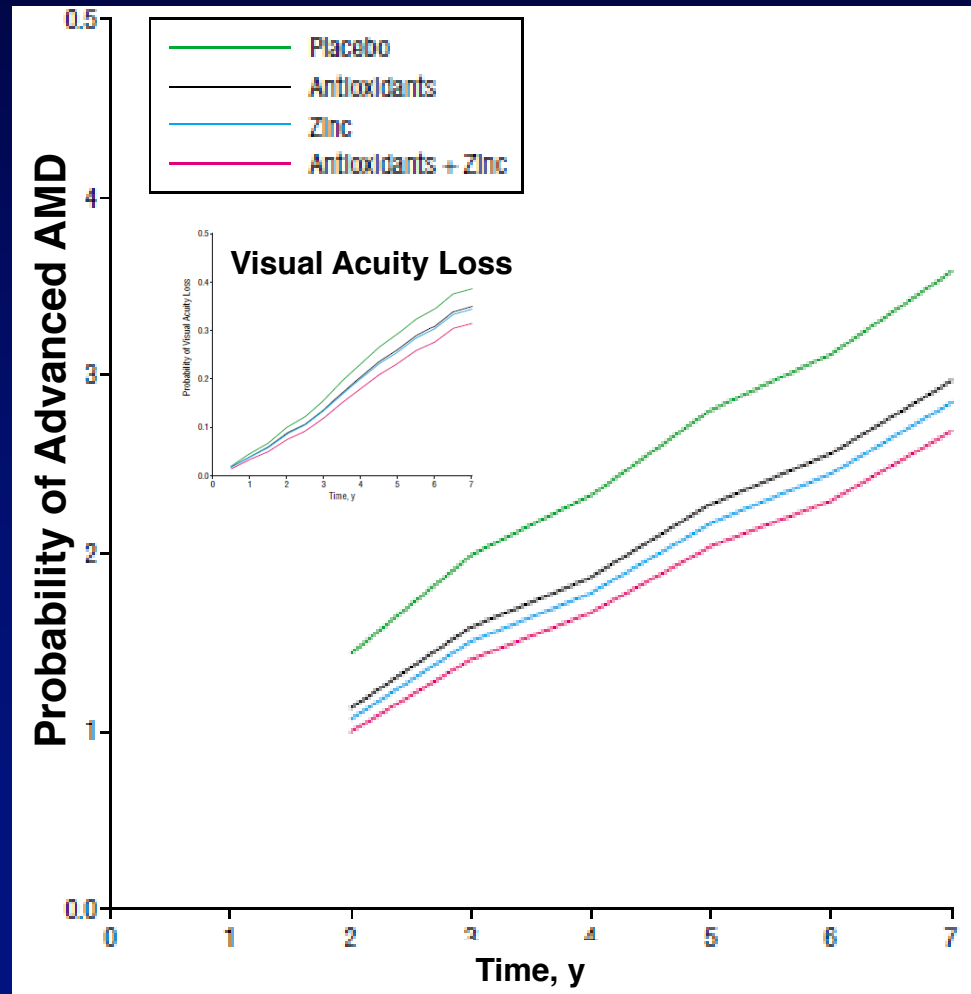
## *Age-Related Eye Disease Study*

### RCT

- n, 4757
- age, 55-80 y
- F/U, 7 y

### SUPPLEMENT

- Vitamin E, 400 IU
- Vitamin C, 500 mg
- $\beta$ -Carotene, 15 mg
- Zinc, 80 mg
- Copper, 2 mg



# Flavonoid Intake at Midlife Promotes Healthy Aging in Women

## *Nurses' Health Study*

---

### Prospective Cohort

- n, 13,818
- age, 74 y
- F/U, 15 y

### *Healthy Aging Criteria*

- Survive to  $\geq 70$  y
- No major chronic diseases
- No major physical impairments  
in cognitive, physical function  
or mental health

# Flavonoid Intake at Midlife Promotes Healthy Aging in Women

## *Nurses' Health Study*

---

***1517 of 13,818 women (11%)  
met criteria for healthy aging***

| <u>Flavonoid</u> | <u>OR</u> |
|------------------|-----------|
| Flavonols        | 18% ↑     |
| Flavones         | 32% ↑     |
| Flavanones       | 28% ↑     |
| Anthocyanins     | 25% ↑     |
| Total Flavonoids | 47% ↑     |

# Anthocyanins Reduce the Risk of Incident Hypertension and Myocardial Infarction

## *Nurses Health Study II*

---

|                      |                 |                 |
|----------------------|-----------------|-----------------|
| <b>n</b>             | <b>87,242</b>   | <b>93,600</b>   |
| <b>Age, y</b>        | <b>25-42</b>    | <b>25-42</b>    |
| <b>F/U, y</b>        | <b>14</b>       | <b>18</b>       |
| <b>Q1 – Q5, mg/d</b> | <b>5.7-21.9</b> | <b>2.5-25.1</b> |

| <u><b>Quintile</b></u> | <u><b>iHT</b></u>    | <u><b>MI</b></u>    |
|------------------------|----------------------|---------------------|
| <b>1</b>               | <b>--</b>            | <b>--</b>           |
| <b>2</b>               | <b>6% ↓</b>          | <b>20% ↓</b>        |
| <b>3</b>               | <b>7% ↓</b>          | <b>29% ↓</b>        |
| <b>4</b>               | <b>9% ↓</b>          | <b>15% ↓</b>        |
| <b>5</b>               | <b>13% ↓</b>         | <b>32% ↓</b>        |
| <b><i>P</i></b>        | <b><i>0.0001</i></b> | <b><i>0.047</i></b> |



# Healthy Aging as Outcome Criteria

## SU.VI.MAX 2

### RCT

- n, 3996
- age,  $65.3 \pm 4.5$  y
- intervention, 8 y
- F/U, 15 y

### SUPPLEMENT

- Vitamin C, 120 mg
- Vitamin E, 30 mg
- $\beta$ -carotene, 6 mg
- Selenium 100  $\mu$ g
- Zinc, 20 mg

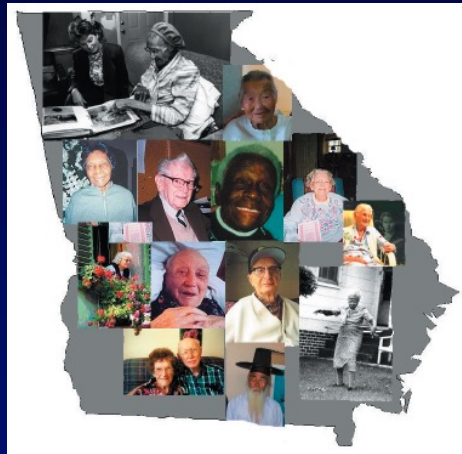
| Criteria <sup>a</sup>                        | Definition   | Corresponding Rowe and Kahn Criterion <sup>b</sup>       |
|--|--|--|
| Good physical functioning                    | SPPB $\geq 11$ of 12   | Maintenance of high physical and cognitive function      |
| Good cognitive functioning                   | MMSE $\geq 27$ , RI-48 $\geq 19$ of 48, and DK-TMT $\geq 5.5$            | Maintenance of high physical and cognitive function      |
| No limitations in IADL                       | <1 limitation  | Avoiding disease and disability                          |
| No depressive symptoms                       | CES-D <16 of 60  |  |
| No health-related limitations in social life | SF-36 responses: 1–2 for item 6 and 3–5 for item 10                      | Sustained engagement in social and productive activities |
| Good overall self-perceived health           | SF-36 responses: 1–3 for item 1  |  |
| No function-limiting pain                    | SF-36 responses: 1–3 for item 7 and 1–2 for item 8                       | Avoiding disease and disability                          |
| No incident major chronic disease            | No incident diabetes, cancer, or cardiovascular disease during follow-up | Avoiding disease and disability                          |

# Antioxidant Supplementation as a Predictor of Healthy Aging

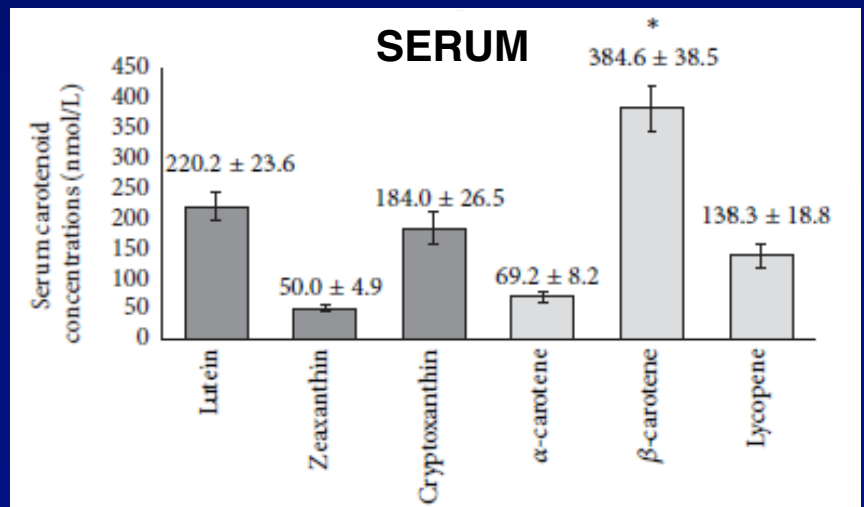
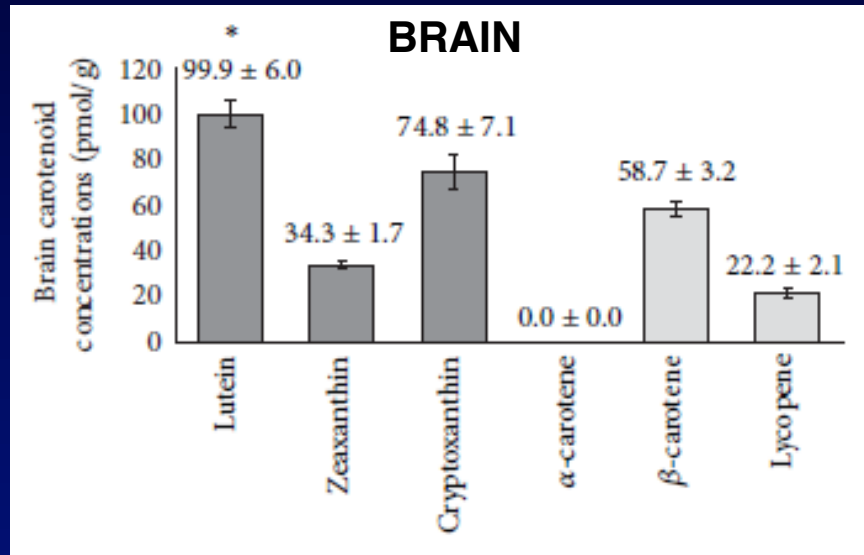
| <u>Stratification Variable</u>          | <u>Total n</u> | <u>RR</u> |
|---|----------------|-----------|
| All participants                        | 3996           | 7% ↑      |
| Men                                     | 2027           | 16% ↑     |
| Vitamin C status, <42 $\mu\text{mol/L}$ | 727            | 28% ↑     |
| Zinc status, <11.9 $\mu\text{mol/L}$    | 953            | 26% ↑     |
| F&V (<400 g/d)                          | 1757           | 17% ↑     |

# Lutein is Concentrated in Brain and Correlated with Cognitive Performance in Elderly

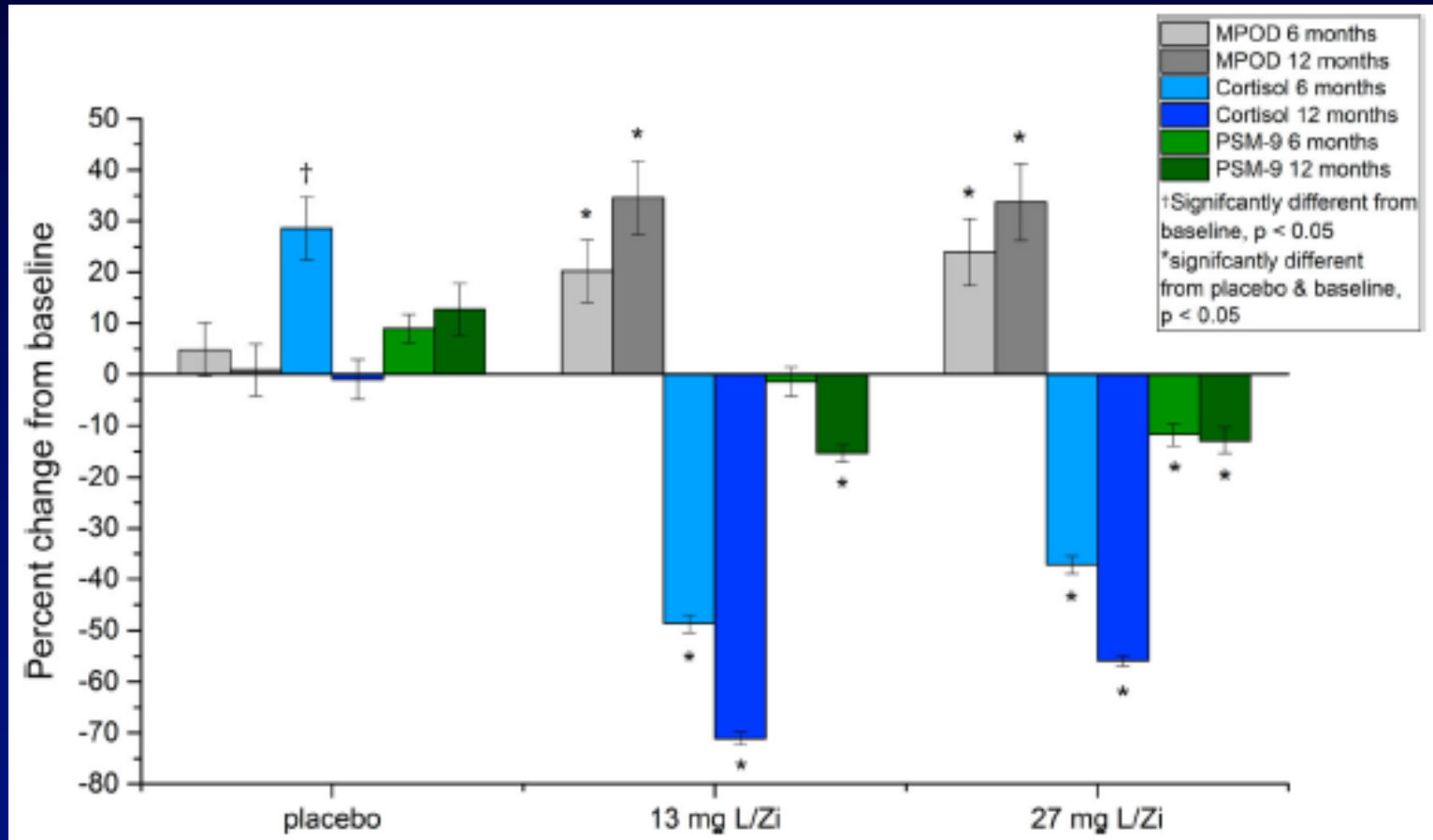
## *The Georgia Centenarian Study*



|                                      | MMSE               |
|--------------------------------------|--------------------|
| Lutein ( <i>trans</i> + <i>cis</i> ) | 0.494 <sup>a</sup> |
| Zeaxanthin                           | 0.439              |
| Cryptoxanthin                        | -0.056             |
| $\beta$ -Carotene, <i>trans</i>      | 0.265              |
| Lycopene, <i>trans</i>               | 0.124              |
| $\alpha$ -Tocopherol                 | 0.393              |
| Retinol                              | 0.161              |

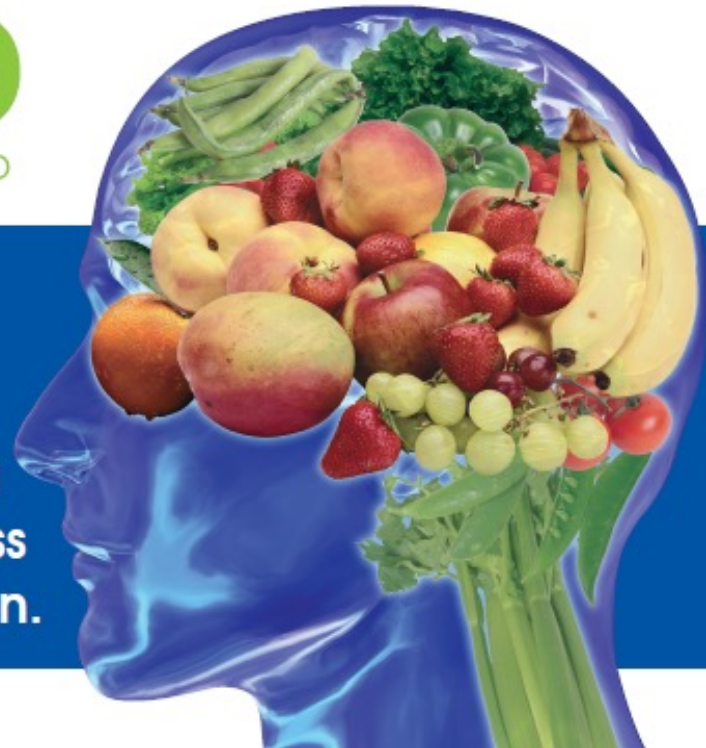


# Lutein/Zeaxanthin Supplementation Reduces Psychological Stress and Serum Cortisol



**RCT** • n, 59  
• age, 21.5 y  
• BMI, <27.0

Depression is one of the most prevalent and disabling disorders in the EU. MooDFOOD is one of the largest consortia investigating depression, and the first to address the role of nutrition in its prevention.



## ABOUT:

### RCT

- n, 1000
- age, 18-75 y
- BMI, 25-40
- duration, 12 mo

### Supplement

- EPA + DHA, 1412 mg
- calcium, 100 mg
- selenium 30  $\mu$ g
- folic acid, 400  $\mu$ g
- vitamin D3, 20  $\mu$ g



# The Secret of Healthy Aging



# The Role of Essential Nutrients in the Continuum of Health

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**Sick**



**Not Sick**



**Well**

# **WHO - Active Ageing: A Policy Framework**

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- **Prevent and reduce the burden of excess disabilities, chronic disease and premature mortality**
- **Reduce risk factors associated with major diseases and increase factors that protect health throughout the life course**
- **Develop a continuum of affordable, accessible, high-quality and age-friendly health and social services that address the needs and rights of people as they age**
- **Provide training and education to caregivers**



