

Impact of Phytonutrients on Inflammation



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TIME

BUSH'S
MILITARY RECORDS
IS DISNEY MOUSETRAPPED?

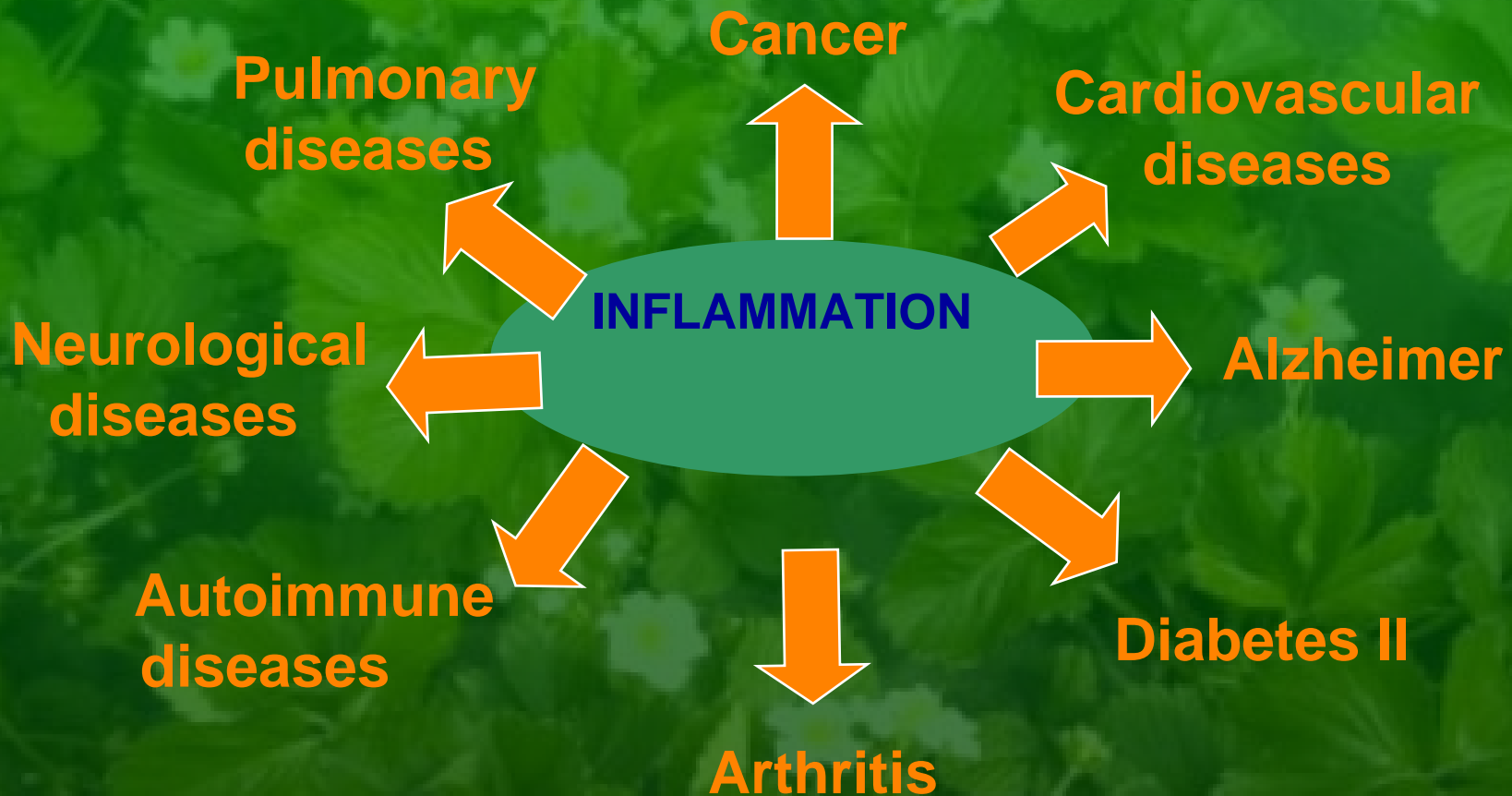
THE SECRET KILLER

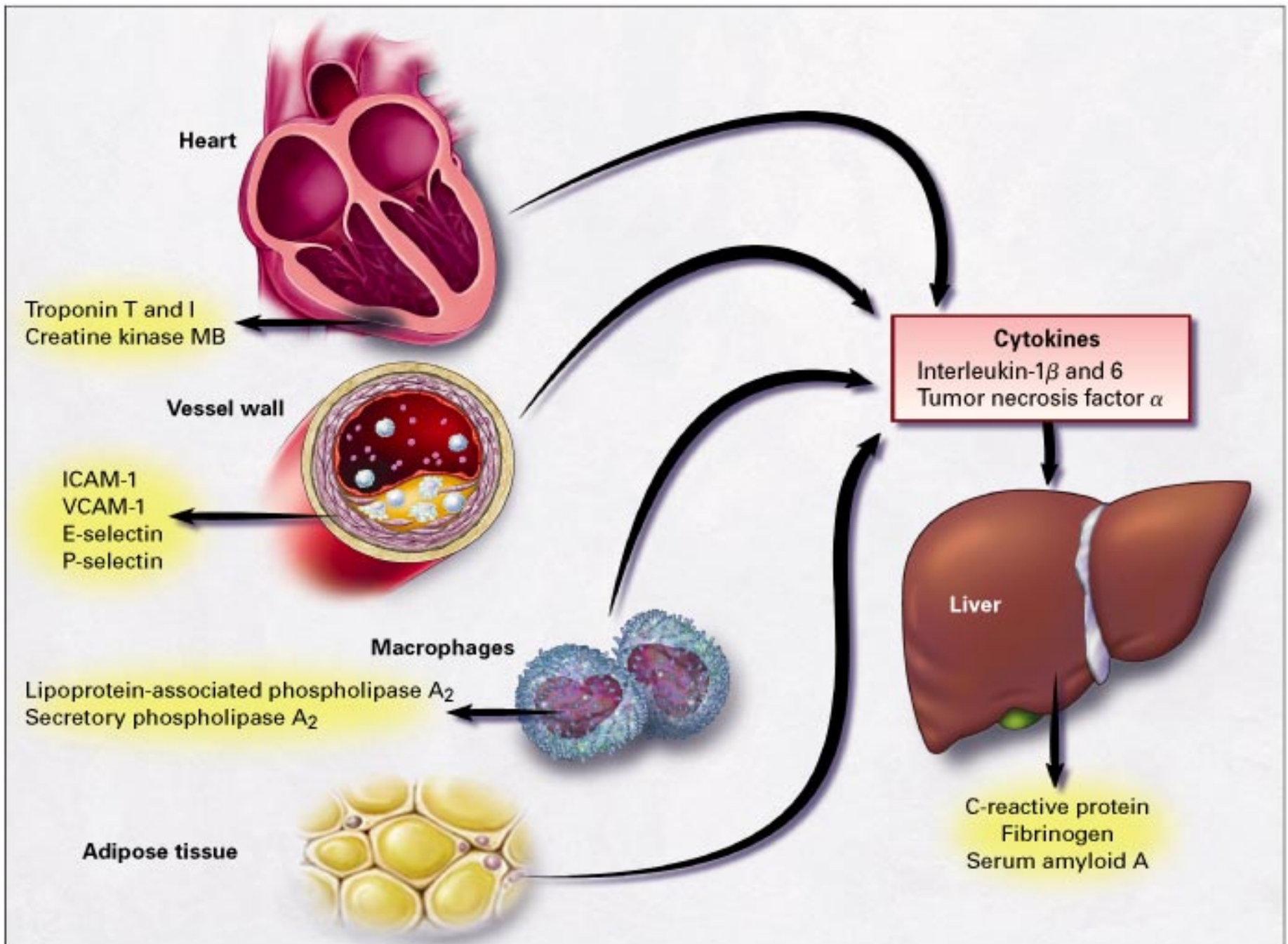
- The surprising link between **INFLAMMATION** and **HEART ATTACKS, CANCER, ALZHEIMER'S** and other diseases
- What you can do to fight it

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TIME Feb. 23, 2004

Role of Inflammation in Human Diseases

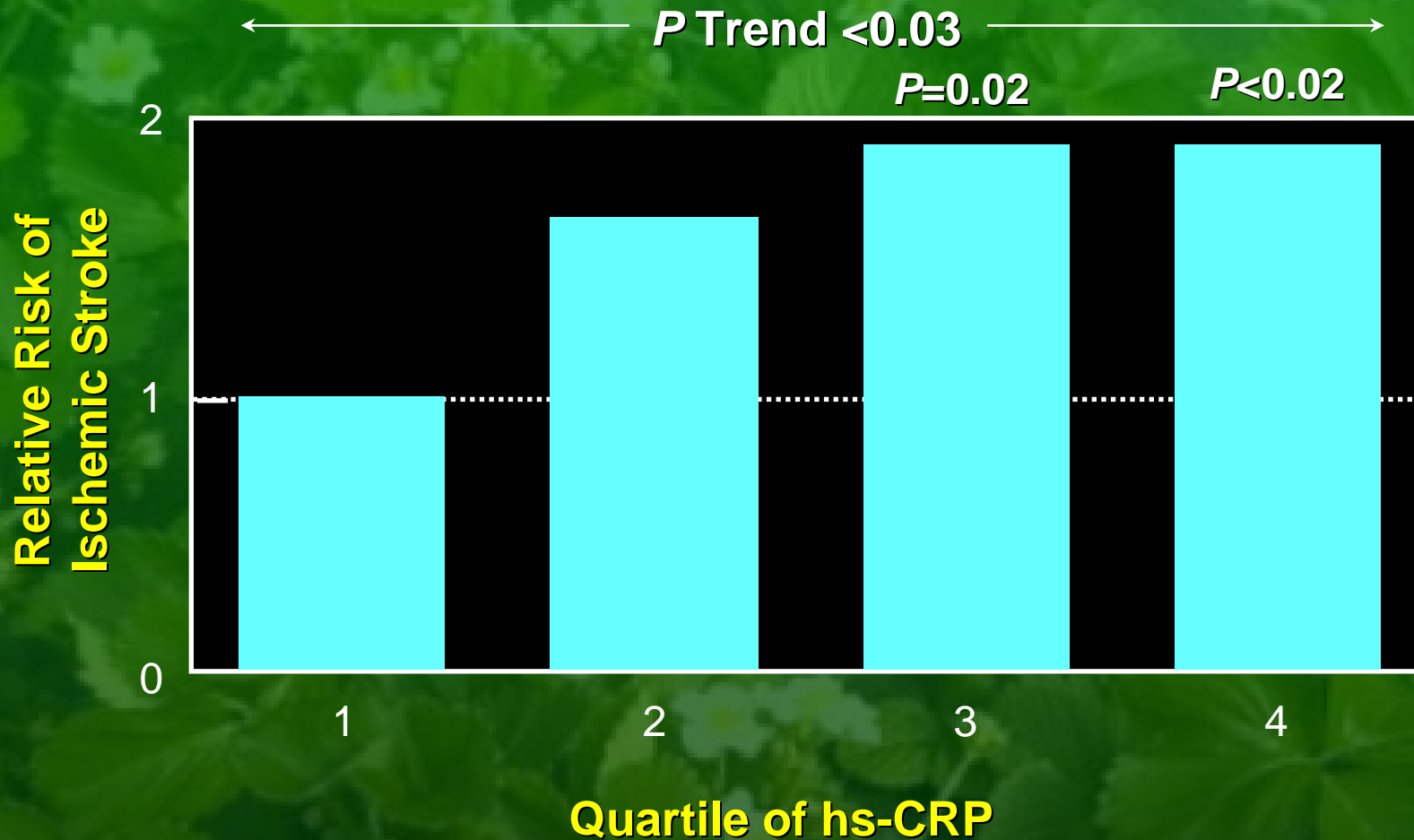




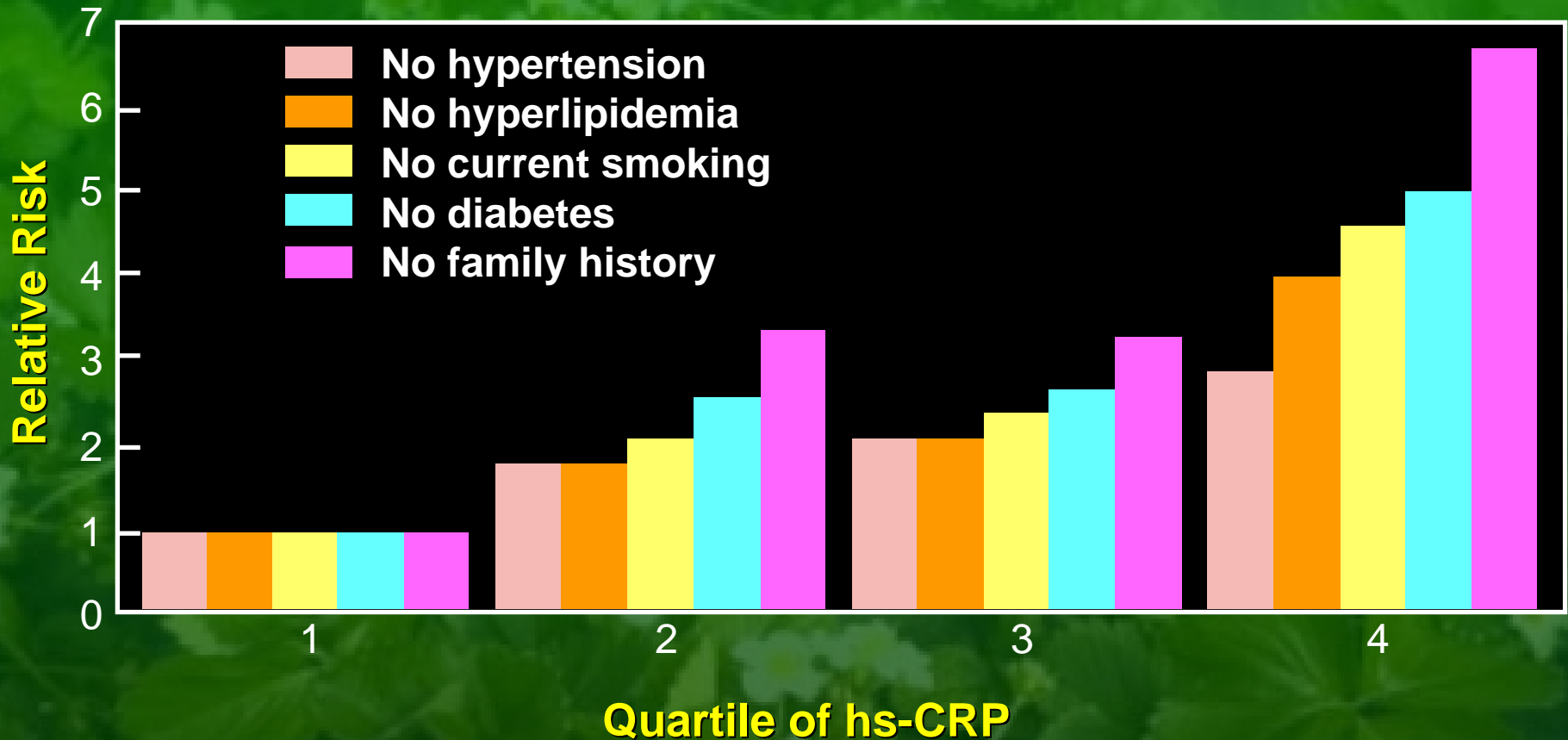
CRP vs hs-CRP

- CRP is an acute-phase protein produced by the liver in response to cytokine production (IL-6, IL-1, tumor necrosis factor) during tissue injury, inflammation, or infection.
- **Standard CRP** tests determine levels which are increased up to 1,000-fold in response to infection or tissue destruction, but cannot adequately assess the normal range
- **High-sensitivity CRP** (hs-CRP) assays (i.e. Dade Behring) detect levels of CRP within the normal range, levels proven to predict future cardiovascular events.

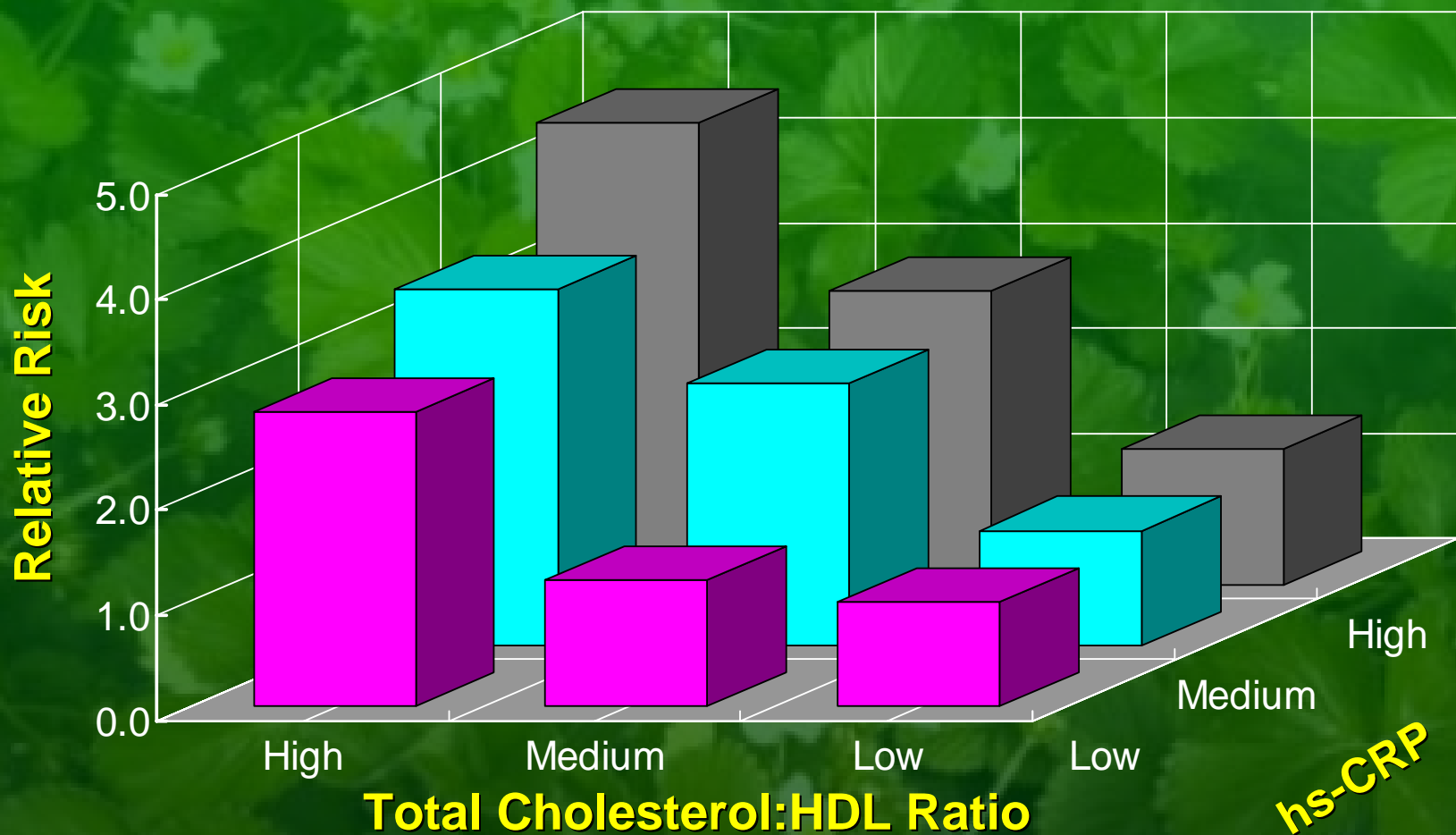
hs-CRP and Risk of Future Stroke in Apparently Healthy Men



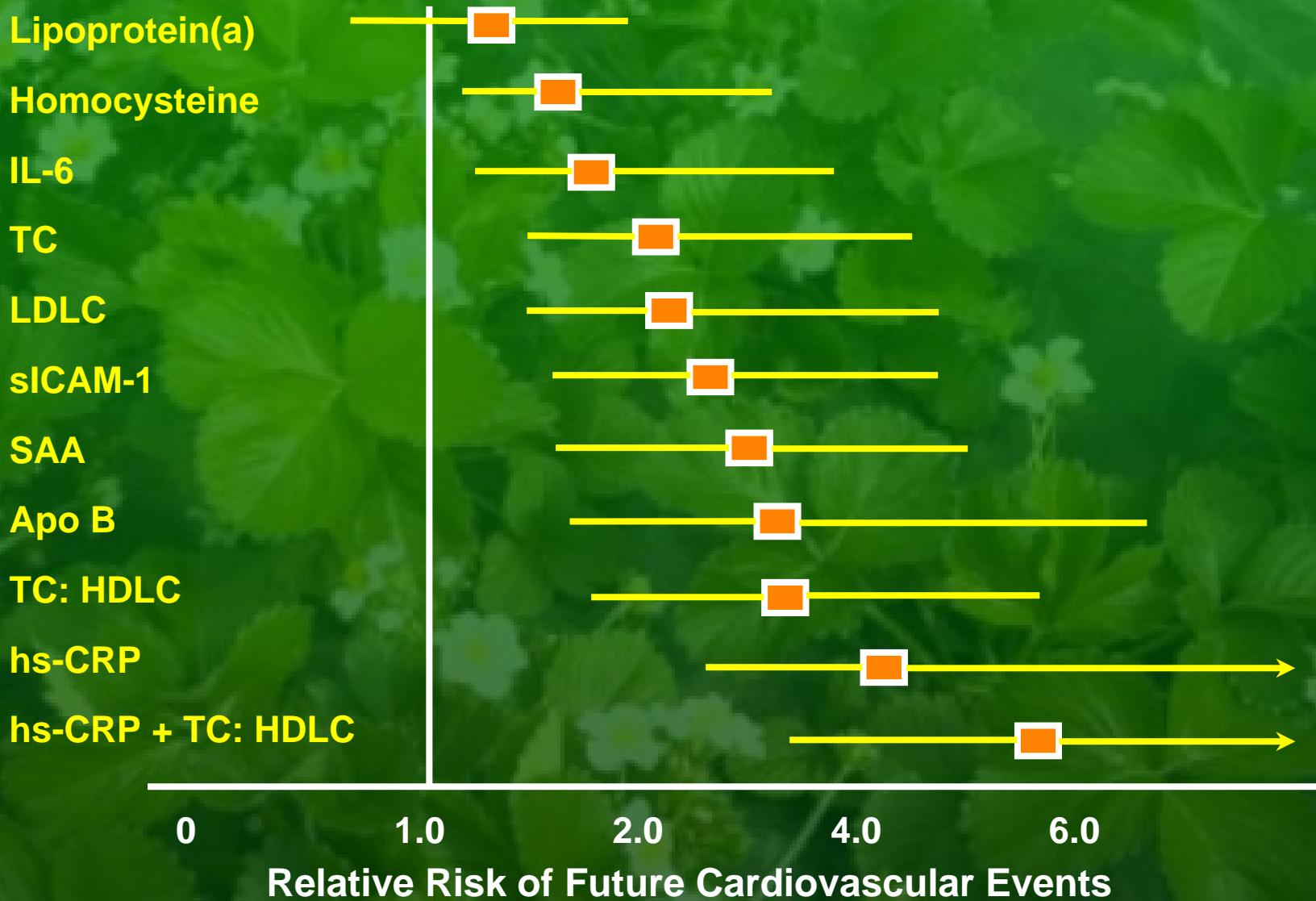
hs-CRP and Risk of Future Cardiovascular Events in Apparently Healthy Women: Low-Risk Subgroups



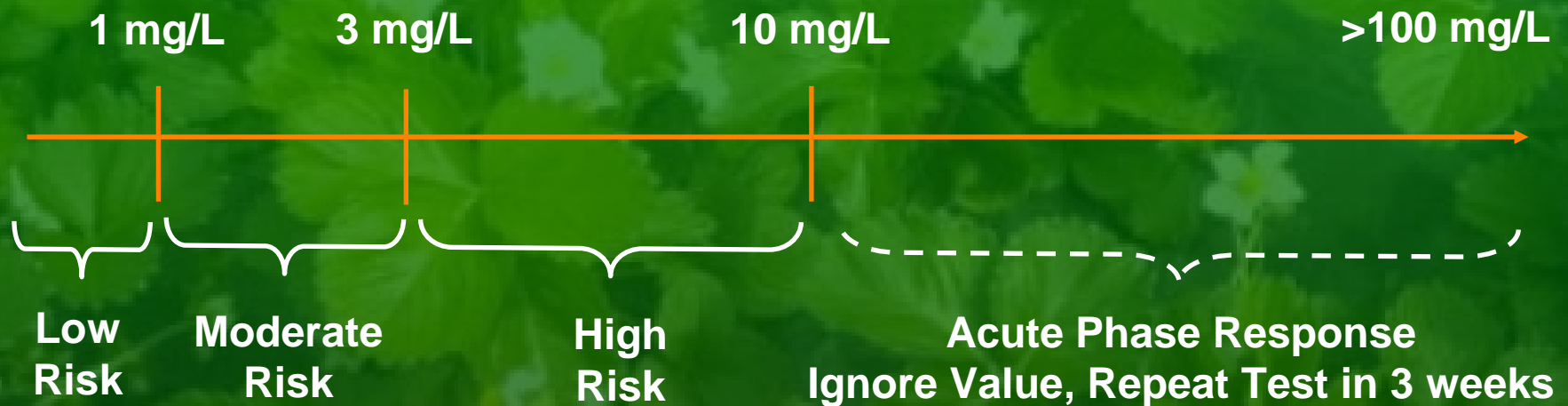
hs-CRP Adds to Predictive Value of TC:HDL Ratio in Determining Risk of First MI



Risk Factors for Future Cardiovascular Events: WHS



Clinical Application of hs-CRP for Cardiovascular Risk Prediction



Similar DNA, different diets!



Diets Then and Now

50,000 Years Ago

- Fruits, nuts, seeds, roots, tubers, flowers, leaves, stalks, beans
- 1/2 the fat
- 2-3x the protein
- No dairy or refined flour
- No processed foods
- No alcohol, no tobacco

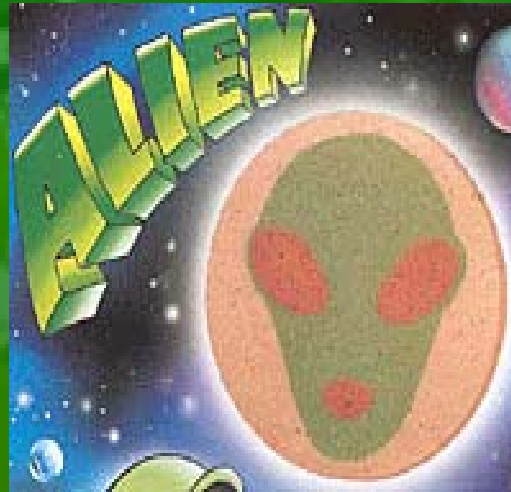
Today

- Potato, refined pasta & cereals white rice & flour, corn
- Added fat and sugar
- High fat proteins
- Ice cream, cheese and whole milk
- Processed foods

Instead of these colors.....



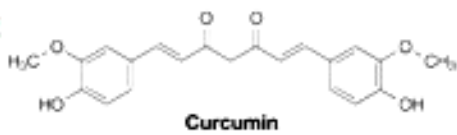
We eat these colors...



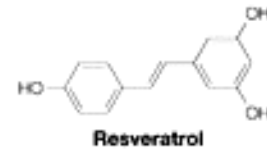
Phytochemicals/Phytonutrients

- Non-nutrient plant compounds
- provide health benefits against certain chronic human illnesses such as cancer, heart disease, neurodegenerative diseases etc.

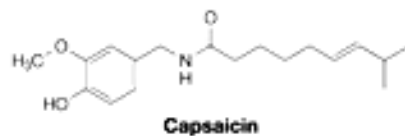
Turmeric



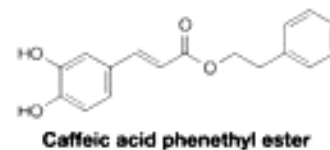
Grapes



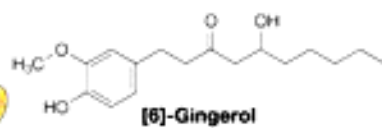
Chili peppers



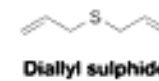
Honey



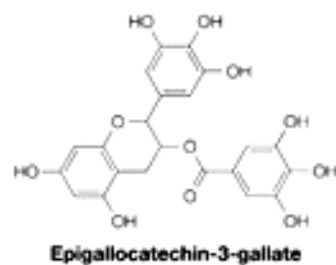
Ginger



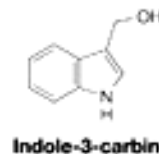
Garlic



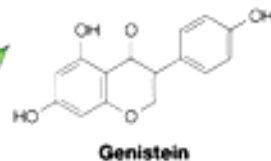
Green tea



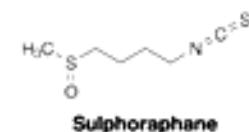
Cabbage



Soybeans



Broccoli



Tomatoes



Phytonutrients and CRP

1. Esposito, K. et al. *Effect of a mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial.* JAMA. 2004; 292;1440-6.
2. Cao. X. et al. *Plasma C-reactive protein and homocysteine concentrations are related to frequent fruit and vegetable intake in Hispanic and non-Hispanic white elders.* J Nutr. 2004;134; 913-8.
3. Block G. et al. *Plasma C-reactive protein concentrations in active and passive smokers: influence of antioxidant supplementation.* J Am Coll Nutr. 2004.
4. King, DE; *Dietary fiber, inflammation and cardiovascular diseases;* Mol. Nutr. Food Res, 2005.

CV benefits of Mediterranean diet on metabolic syndrome

| End Point | Mediterranean diet | Control | P value |
|--------------|--------------------|---------|---------|
| Weight (kg) | -4 | -1.2 | <0.001 |
| CRP (mg/L) | -1.1 | -0.1 | 0.01 |
| IL-6 (pg/mL) | -0.7 | -0.1 | 0.04 |

55% on Mediterranean diet no longer had MS

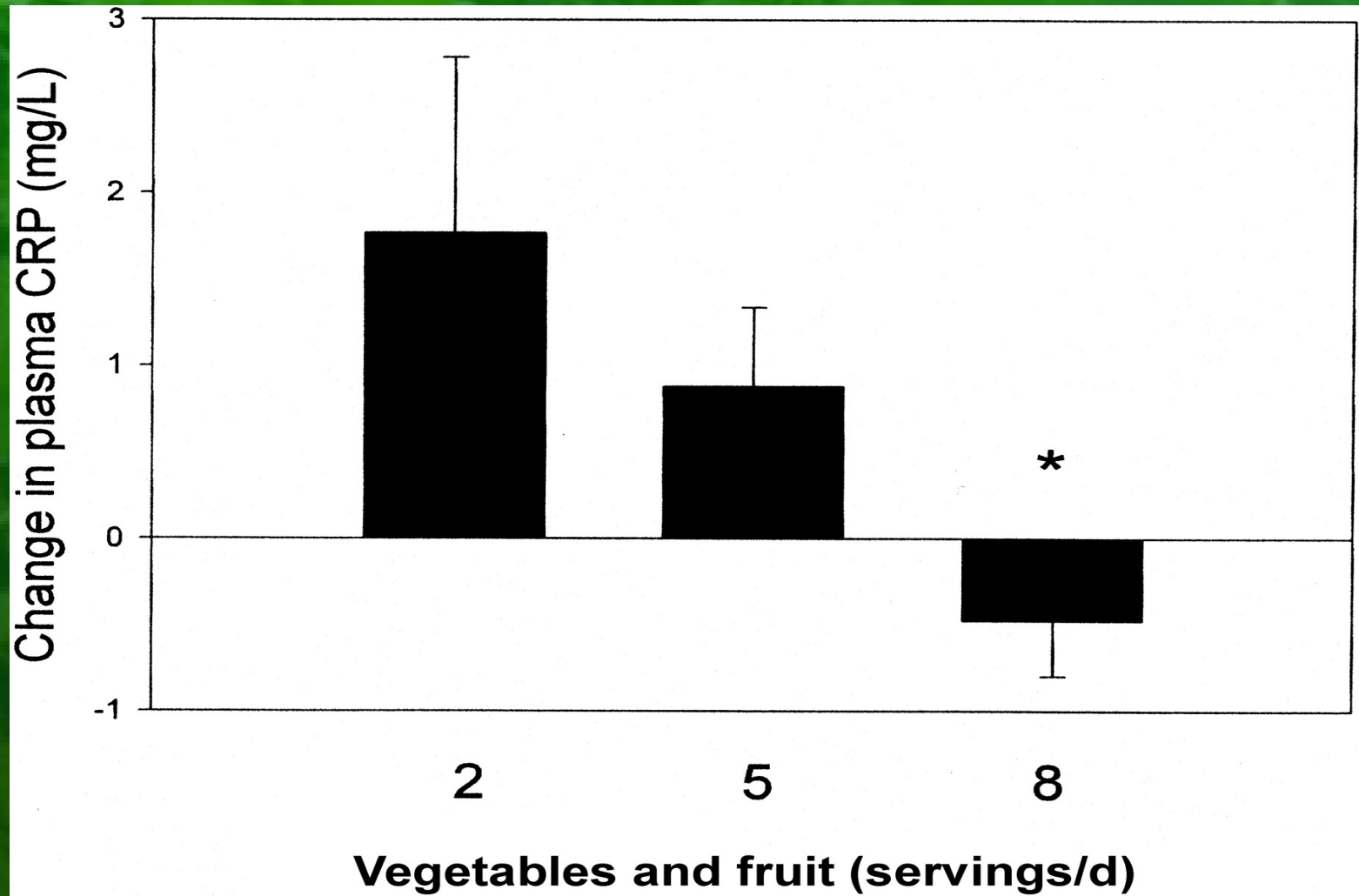
Fruit and Vegetable Intake and Inflammation Markers

Fruit intake (d/w)

Vegetable intake (d/w)

| | <1 (n = 286) | 1-2 (n = 436) | 3-4 (n = 584) | 5-6 (n = 609) | 7 (n = 1164) | <i>P</i> for trend ² | <1 (n = 95) | 1-2 (n = 383) | 3-4 (n = 886) | 5-6 (n = 947) | 7 (n = 810) | <i>P</i> for trend ² |
|--|-------------------------|------------------------|-------------------------|------------------------|-------------------------|---------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------------------------------|
| Plasma vitamin C (μmol/L) ³ | 15.3 (13.7, 16.9) | 18.2 (16.8, 19.7) | 19.5 (18.0, 20.9) | 24.5 (23.3, 26.3) | 27.9 (26.6, 29.4) | <0.0001 | 14.9 (12.3, 18.0) | 18.9 (17.5, 20.9) | 20.7 (19.7, 22.2) | 24.5 (23.3, 26.3) | 25.3 (24.1, 27.1) | <0.0001 |
| CRP (mg/L) ³ | 1.84 (1.62, 2.08) | 1.72 (1.55, 1.90) | 1.68 (1.54, 1.82) | 1.55 (1.42, 1.68) | 1.51 (1.42, 1.62) | 0.002 | 1.73 (1.39, 2.16) | 1.55 (1.39, 1.73) | 1.69 (1.58, 1.82) | 1.63 (1.52, 1.73) | 1.51 (1.40, 1.63) | 0.15 |
| t-PA (ng/mL) | 11.13 (10.65, 11.61) | 11.11 (10.73, 11.5) | 10.98 (10.65, 11.31) | 10.18 (9.86, 10.50) | 10.59 (10.36, 10.82) | 0.001 | 11.37 (10.53, 12.20) | 11.00 (10.59, 11.40) | 10.87 (10.58, 11.11) | 10.46 (10.20, 10.71) | 10.69 (10.40, 10.96) | 0.03 |

High Intake of Carotenoid-rich Vegetables and Fruit Reduces Plasma CRP



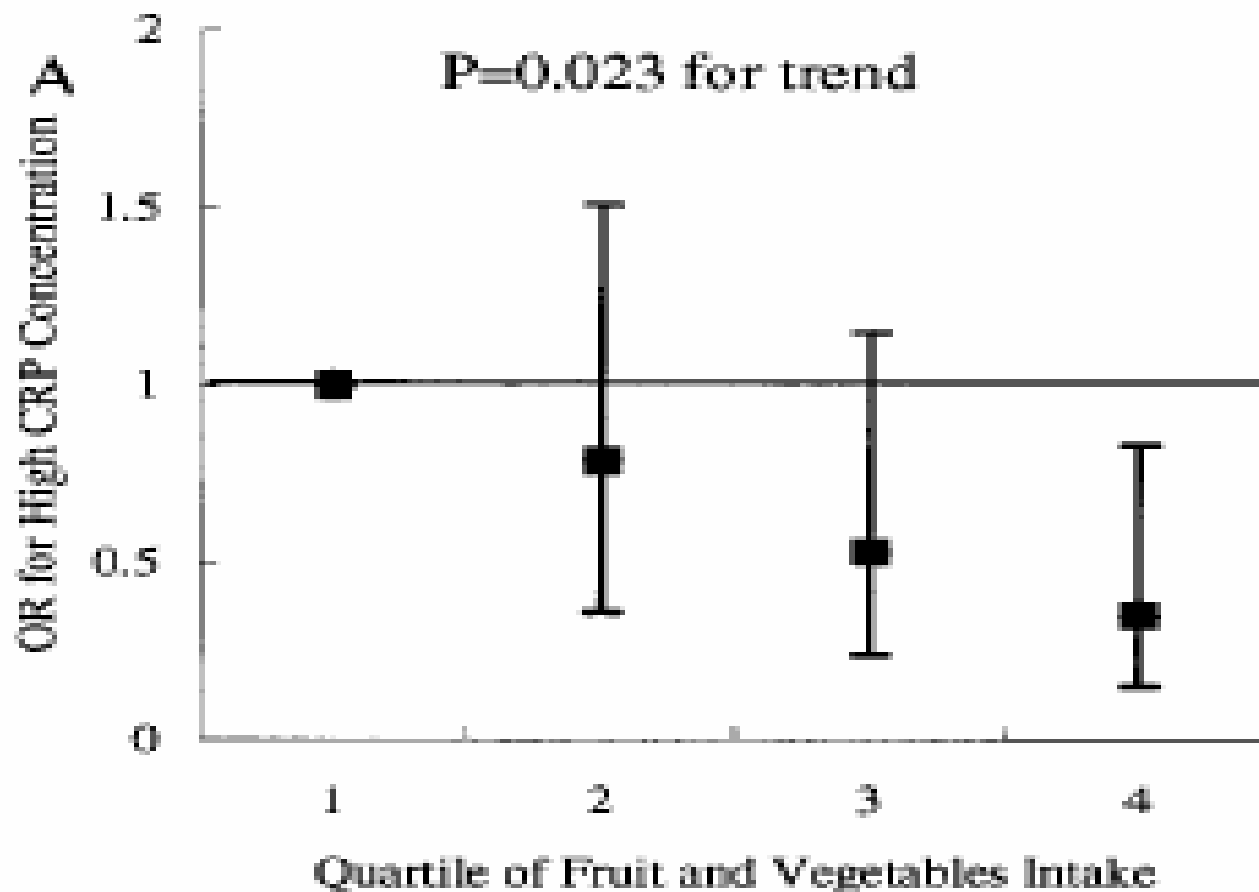
Dietary Patterns and Inflammation Markers in MESA

| Factor 1: fats and processed meats | Q1 | Q2 | Q3 | Q4 | Q5 | <i>P</i> for trend ² |
|------------------------------------|-------------|-------------|-------------|-------------|-------------|---------------------------------|
| CRP (mg/L) | 1.52 ± 1.04 | 1.71 ± 1.04 | 1.81 ± 1.04 | 1.99 ± 1.04 | 2.02 ± 1.05 | < 0.001 |
| IL-6 (pg/mL) | 1.09 ± 1.02 | 1.15 ± 1.02 | 1.16 ± 1.02 | 1.21 ± 1.02 | 1.26 ± 1.03 | < 0.001 |
| Homocysteine (μmol/L) | 8.60 ± 1.01 | 8.69 ± 1.01 | 8.80 ± 1.01 | 8.84 ± 1.01 | 8.95 ± 1.01 | 0.004 |
| sICAM-1 (ng/mL) | 265 ± 1.01 | 257 ± 1.01 | 261 ± 1.01 | 253 ± 1.01 | 254 ± 1.02 | 0.21 |
| sE selectin (ng/mL) | 49.7 ± 1.05 | 44.3 ± 1.04 | 49.0 ± 1.04 | 48.5 ± 1.04 | 46.6 ± 1.05 | 0.80 |

Dietary Patterns and Inflammation Markers in MESA

| Factor 4: whole grains and fruit | Q1 | Q2 | Q3 | Q4 | Q5 | <i>P</i> for trend ² |
|----------------------------------|-------------|-------------|-------------|-------------|-------------|---------------------------------|
| CRP (mg/L) | 1.96 ± 1.04 | 1.99 ± 1.04 | 1.80 ± 1.04 | 1.74 ± 1.04 | 1.55 ± 1.04 | < 0.001 |
| IL-6 (pg/mL) | 1.26 ± 1.02 | 1.21 ± 1.02 | 1.16 ± 1.02 | 1.11 ± 1.02 | 1.12 ± 1.02 | < 0.001 |
| Homocysteine (μmol/L) | 8.97 ± 1.01 | 8.89 ± 1.01 | 8.73 ± 1.01 | 8.68 ± 1.01 | 8.58 ± 1.01 | < 0.001 |
| sICAM-1 (ng/mL) | 262 ± 1.01 | 256 ± 1.01 | 258 ± 1.01 | 259 ± 1.01 | 253 ± 1.01 | 0.044 |
| sE selectin (ng/mL) | 49.6 ± 1.04 | 47.2 ± 1.04 | 49.5 ± 1.04 | 46.3 ± 1.04 | 46.3 ± 1.04 | 0.26 |

Fruit and Vegetable Intake in Hispanic and Non-Hispanic White Elders



Pooled Risks of Stroke in Meta-analysis According to Study Variables

| Variable | Cohorts, n | Participants, n (events, n) | Fruit and vegetable intake | | |
|----------------------------------|------------|--------------------------------|----------------------------|------|------|
| | | | <3 | 3-5 | >5 |
| Sex | | | | | |
| ● Men | 5 | 81 530 (1949) | 1 | 0.83 | 0.71 |
| ● Women | 2 | 99 067 (1600) | 1 | 0.95 | 0.76 |
| Duration of follow-up | | | | | |
| ● <10 y | 3 | 119 686 (1384) | 1 | 0.85 | 0.75 |
| ● >10 y | 6 | 137 865 (3533) | 1 | 0.92 | 0.73 |
| Dietary assessment method | | | | | |
| ● Food frequency questionnaire | 7 | 256 167 (4778) | 1 | 0.91 | 0.74 |
| ● Other | 2 | 1384 (139) | 1 | 0.70 | 0.60 |

He FJ et al. *Lancet* 2006; 367: 320-326.

Strawberry Research at UCLA

- Identify phytochemicals in strawberries
- Investigate presence of strawberry phytonutrients in human plasma and urine
- Determine biological activities for these phytonutrients in plasma and urine



Strawberry Phenolics

- **Flavanoids**
 - **Anthocyanins: Pelargonidin and Cyanidin**
 - **Flavonols: Quercetin and Kaempferol**
- **Hydrolyzable tannins**
 - **Ellagitannins, Gallotannins, Ellagic Acid, Ellagic Acid Glycosides**
- **Phenolic Acids**
 - **Hydroxycinnamic acids and esters,**



Human Study

Bioactivities of compounds in plasma and urine:

- Inflammation: highly sensitive CRP
- Oxidative damage: *ex-vivo* LDL oxidation; lymphocyte 8-OHDG, urinary isoprostanes
- Phase II enzymes: Serum GST- α , UDP-glucuronosyltransferase and β -glucuronidase activity



CONCLUSIONS

- Fruits and vegetables contain high levels and a wide diversity of phytonutrients
- Phytonutrients in fruits and vegetables were shown to decrease CRP and inflammation