Fruits and Vegetables – Why More Matters

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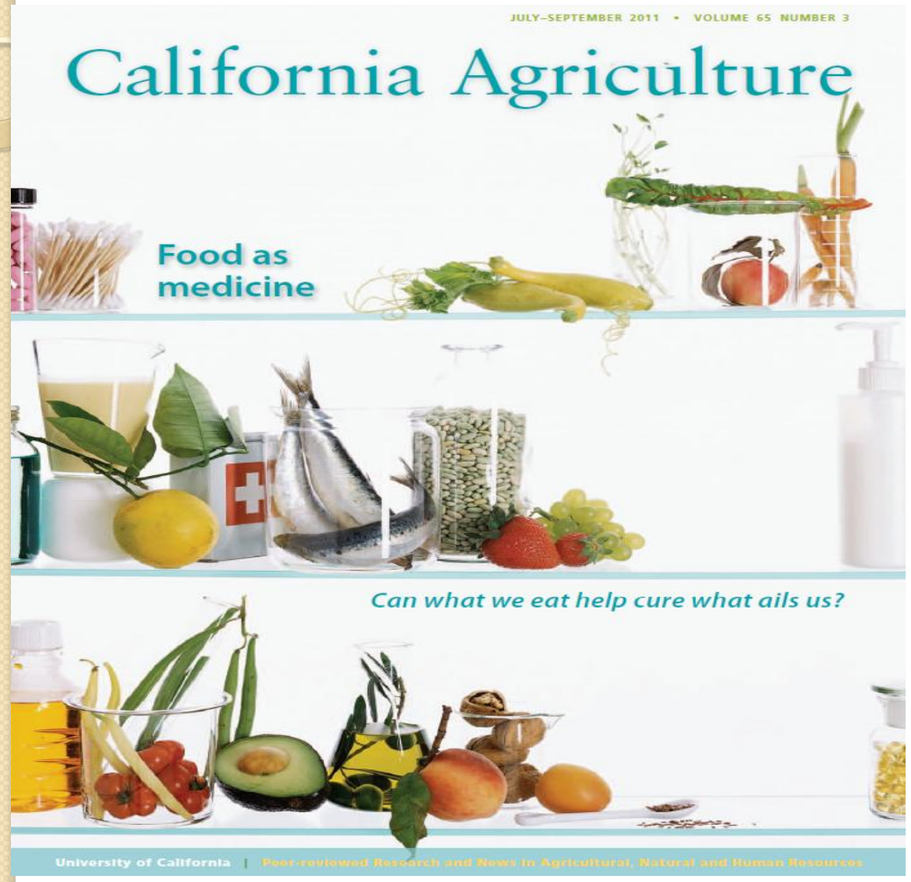
Obesity & Nutrition in a Changing World Symposium

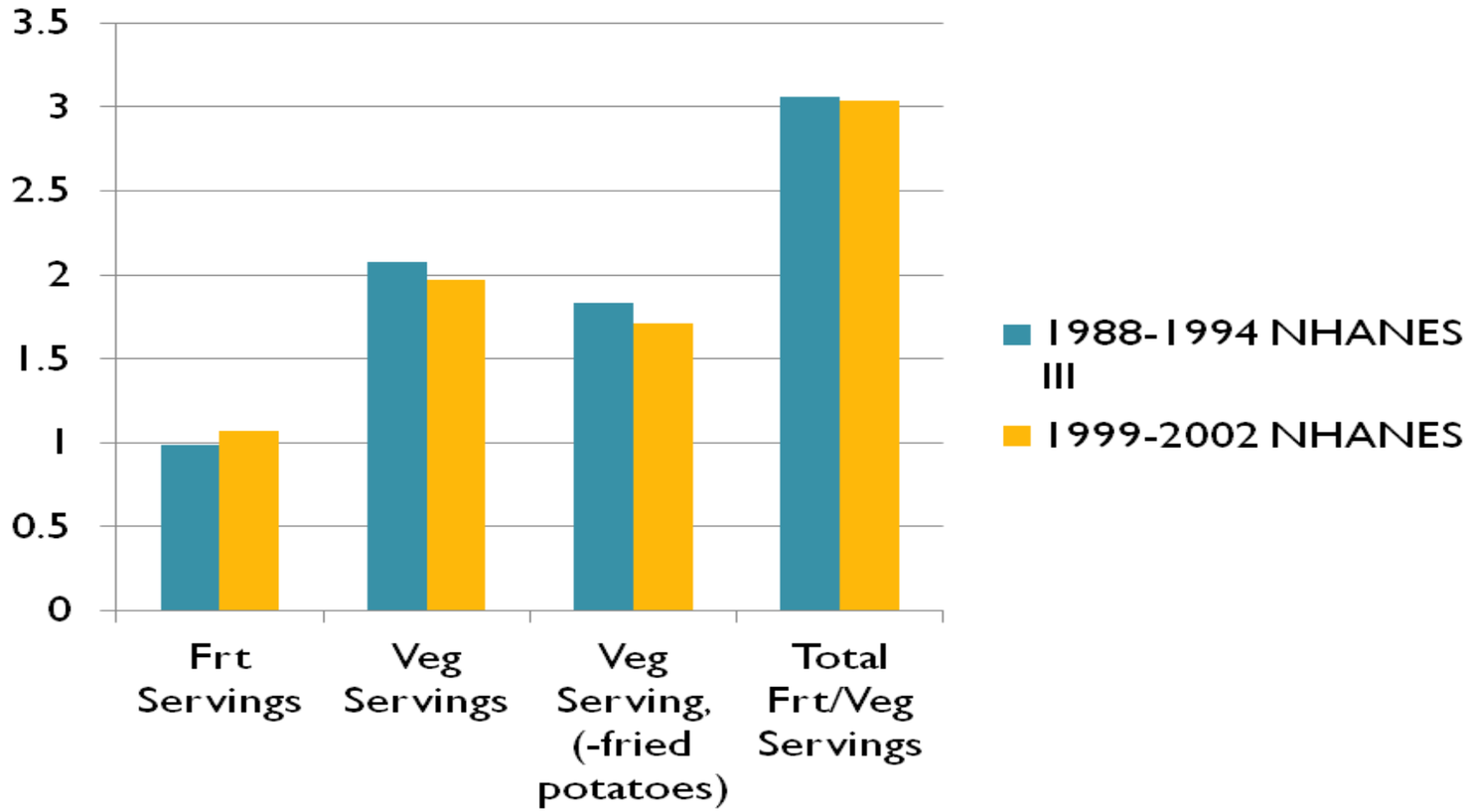
Learning Objectives



Learners will:

- Gain an understanding of usual fruit & vegetable intake
- Be able to define the term dietary "phytonutrient" or "flavonoid "
- Be able to describe the association between fruit & vegetable intake, and positive health outcomes (reduction of chronic disease risk)
- Be able to describe possible mechanisms for how phytonutrient –rich foods promote health
- Be aware of challenges to implement successful interventions to increase fruit & vegetable intake in a

Fruit & Vegetable Intake – US Trends 1988-2002



- 10.8% of population eating ≥2 Fruit & ≥3 Vegetable servings
- 23.6% of population eating ≥5 of any Frt/Veg combination

Casagrande et al. Am J Prev Med 2007 32:257

Fruits & Vegetables and Chronic Disease Risk

- Strong & convincing evidence of ↑ F/V consumption leading to ↓ risk of the following diseases:
  - Hypertension, Coronary Heart Disease, Stroke
- Probable evidence:
  - Cancer, Type 2 diabetes (indirectly through weight control)
- Possible evidence:
  - Obesity, Macular degeneration, Dementia, Asthma & COPD
- Insufficient evidence:
  - Inflammatory bowel diseases, diabetic retinopathy

Slavin & Lloyd 2012 Adv Nutr 3:506
Boeing et al 2012 Eur J Nutr epub ahead of press

Fruits and Vegetables Decrease Cardiovascular Disease Risk & Clinical Outcomes

Multivariate adjusted* Relative Risk for Frt/Veg consumption ≥ 3 times/day vs. <1 time/day

- **Ischemic heart disease mortality RR=0.76 (95% CI: 0.56, 1.03)**
- **CVD mortality RR=0.73 (95% CI: 0.58, 0.92)**
- **All cause mortality RR=0.85 (95% CI: 0.72, 1.00)**

*adjusted for age, sex, race, energy, physical activity, alcohol consumption, smoking, plus others

Bazzano et al AJCN 2002; 76, 93-99

Cross-sectional studies using biomarker outcomes

- F/V intake is correlated with improved inflammatory status in a community setting
  - N=1000, 18-85 y, food intake assessed & blood samples taken
  - Inverse relationship of inflammatory markers with increasing F/V intake
  - *Root et al. Nutrients 2012*

- F/V consumption is related to makers of inflammation and oxidative stress in adolescents
  - N=285, 13-17 y, food intake assessed & blood samples taken
  - Inverse relationship of inflammatory markers with increasing F/V intake
  - *Holt et al. JADA 2009*

Fruits & Veggies contain…

- Vitamins (C, Folate, etc.)
- Minerals (Potassium, Magnesium, etc.)
- Fiber (mostly soluble)
- Bioactive compounds
  - Not traditional nutrients
  - Have biologic activities
    - Examples: Carotenoids (such as lutein, zeaxanthin, lycopene, etc.); Phytochemicals (such as various phenolic compounds – ellagic acid, quercetin, anthocyanidins, etc.)

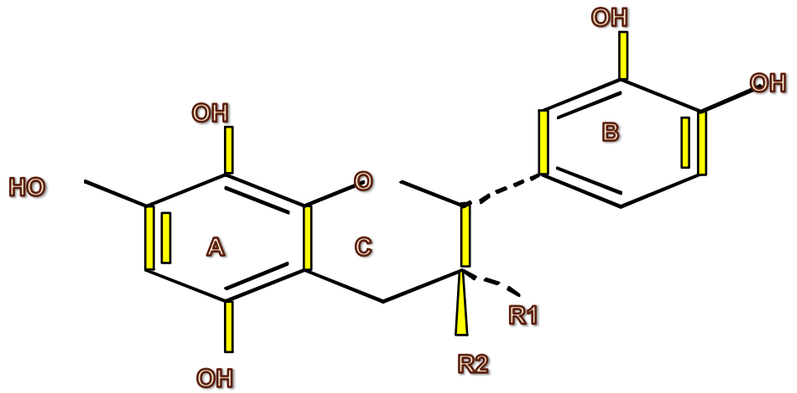
Dietary Phytochemicals

Phytochemicals are a broad and diverse group of phenolic compounds that are produced in and accumulate in plants.

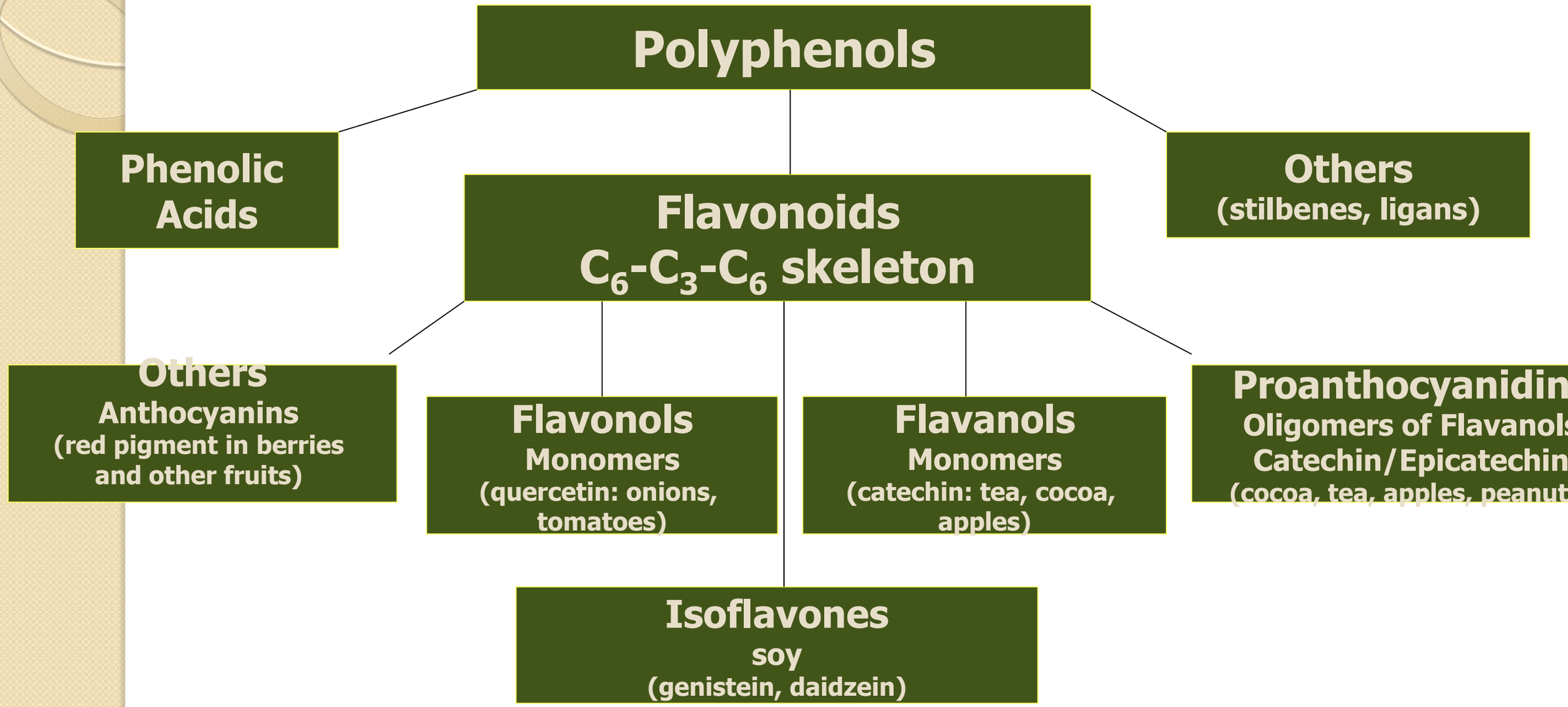
Phytochemical rich foods include: fruits and vegetables, some cocoa products, as well as whole grains and beverages such as tea & wine.

Phytochemicals can alter metabolic & cellular processes.

Most dietary studies indicate that diets rich in phytochemicals are associated with improved health and provide protection against chronic diseases, or alter *in a positive* direction markers for chronic disease.



Phytochemical Nomenclature



Questions about health promoting effects of food flavonoids

- Important issues:
  - Are the phytochemicals absorbed & do they get to target tissues? How much is absorbed?
  - What is the best model to study the effects in?
  - What are the biologic effects on key markers of function or health? (or disease risk)
  - Is the effect the same in healthy or at risk individuals?
  - What is/are the specific bioactive component(s)?
  - How can you monitor intake after consuming the food?
  - What are the implications for human health? Should there be specific dietary recommendations for intake?

Dietary Flavonoids

- Estimated intake: 0.01-1.0 g/day
- Major Dietary sources:
  - Fruits and vegetables such as apple, grapes, onion: rich in flavonols, (quercetin, anthocyanidin, kaempferol)

  - Citrus fruits: rich in flavanols (hesperidin and naringenin)

  - Soy: rich in isoflav stein and Daidzein)

Absorption, Distribution, Metabolism, Excretion (ADME) – Factors which impact biologic effects of phytochemicals

- Intake of phytochemical or precursor does not automatically equate with exposure at tissue level
- Inter-individual differences
  - Transport across intestinal wall
  - Biotransformation enzymes (phase I & II) genetic differences & effects of other endogenous or xenobiotic compounds
  - Intestinal Microbiota
  - Gut transit
  - Age, gender, physiologic state
- Diet, food matrix, chemical nature of polyphenol

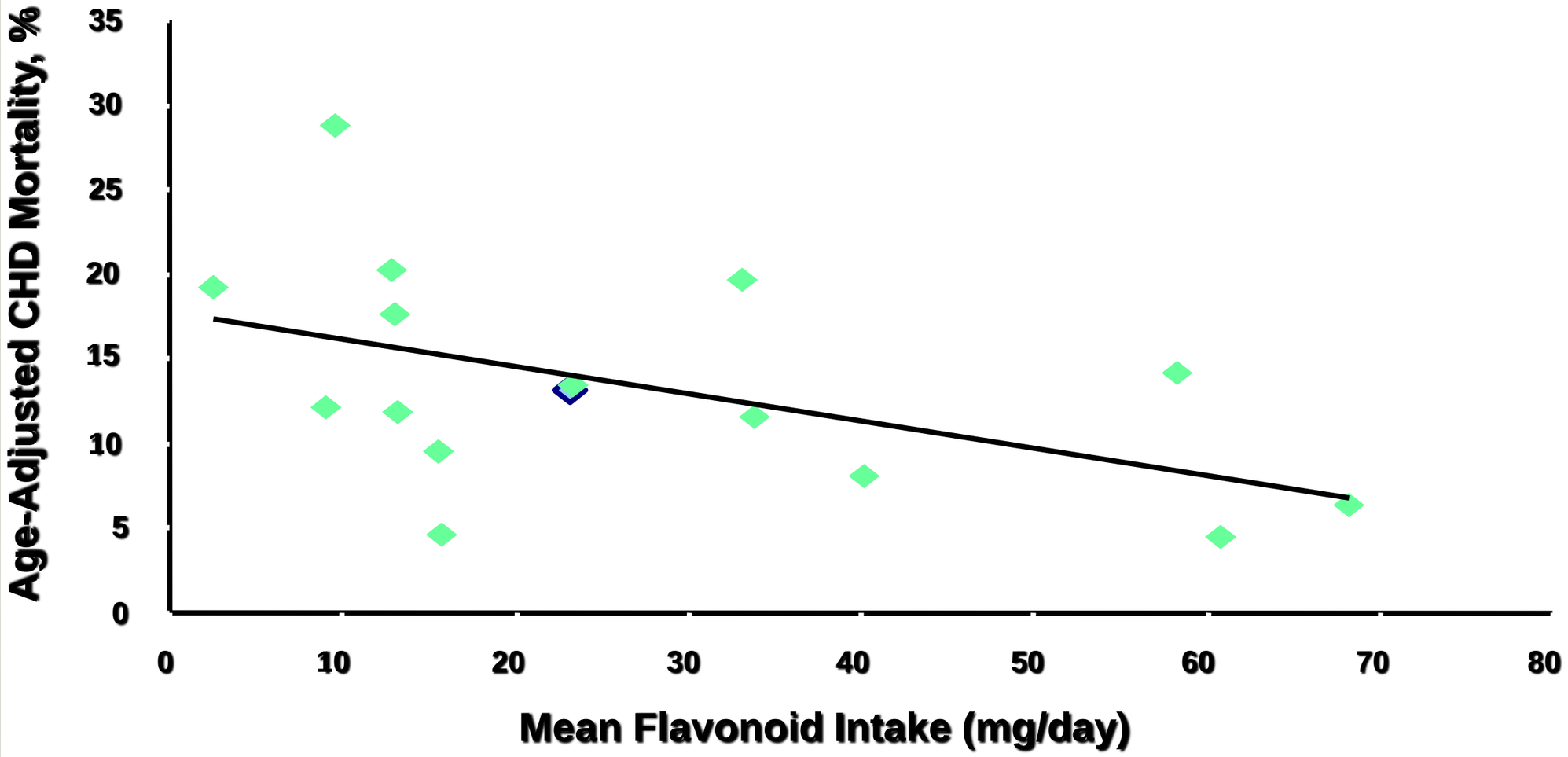
Metabolism of Flavonoids

- Absorbed mainly in aglycone form, possibly some glycosides
- Peak blood levels occur within 1 to 2.5 hours, or up to 8 hours for some compounds
- Plasma concentration in 1-5 μmol/L range
- Circulate in blood as conjugated metabolites (glucuronides and methylated or sulfated)
- Can be partially metabolized by gut microbes
- Elimination half-life of 23 to 28 hours
- Urinary excretion
- Bioavailability of 20% +/-

Dietary polyphenols have been postulated to modulate the development and progression of several chronic diseases:

- Age related vision loss
- Osteoporosis
- Obesity
- **Hypertension**
- **Cardiovascular disease**
- **Diabetes**
- **Cancer**

Flavonoid Intake and Risk of CHD Mortality



Hertog et al. *Arch Intern Med* 155: 381-386, 1995

Flavonoids, Flavonoid-rich Foods & Chronic Disease Risk

- AJCN 2008 Hooper et al. – Meta-Analysis of 133 RCT of various flavonoid food sources on CVD risk
  - Green tea (LDL), cocoa (FMD), soy protein (LDL)
  - Clinically relevant changes observed

- AJCN 2007 Mink et al. – Flavonoids and CVD mortality in Iowa Women's Health Study
  - Found RR for highest vs lowest quintile or any intake vs none for classes of flavonoids between 0.78 and 0.91
  - Individual foods associated w/ risk reduction included bran, apples, pears, red wine, grapefruit, strawberries, chocolate

- Int J Cancer 2008 Cutler et al. – Flavonoids and Cancer Risk in Iowa Women's Health Study
  - Isoflavone intake inversely associated w/ overall cancer incidence
  - Lung cancer incidence inversely associated w/ flavanones & proanthocyanins. Strongest effect in current & past smokers

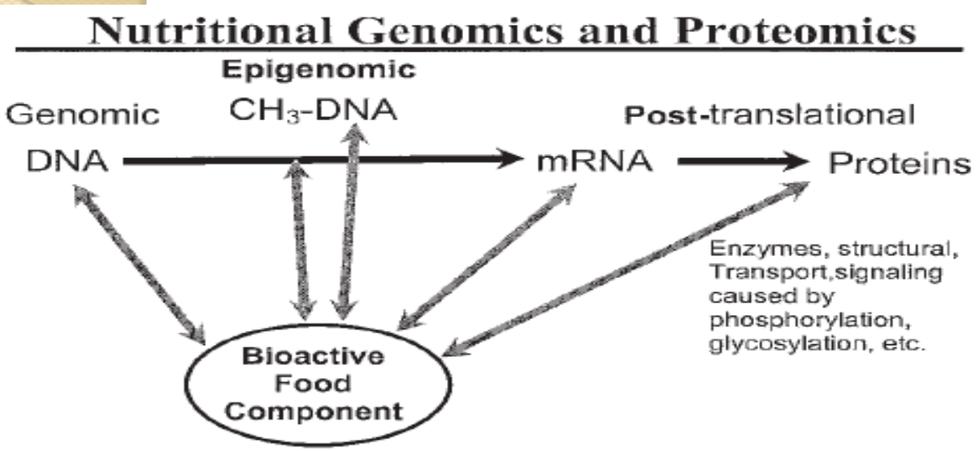
- Nutr Rev 2012 Peterson et al. – Associations between flavonoids and cardiovascular

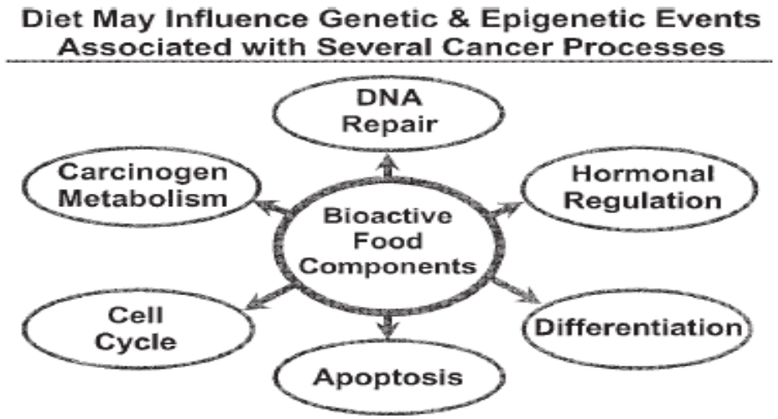
Comments on Epidemiologic vs Clinical Trials for Investigating Health Effects of Flavonoids

- Observational Epidemiologic studies can confirm or negate theories about importance of flavonoids in the diets of free-living individuals
  - Useful to evaluate human health effects of long-term exposure to physiologic concentrations of flavonoids
  - Cannot prove causality
  - Reliable data on flavonoid contents of foods not available for all classes
  - Correlations between flavonoids & other food components is high, therefore difficult to conclude association truly exist w/ the flavonoid alone

- RCT – human clinical studies
  - Aimed at demonstrating physiologic phenomenon in response to foods or to isolated food flavonoid components
  - Important to consider synergisms of food components & other foods in total diet
  - Help to identify potential mechanistic functions
  - Examine biomarkers, not usually clinical endpoints

Phytochemicals (Flavonoids) - Potential Targets and Mechanisms of Action





- Cellular & Molecular Targets
  - Enzyme inhibition or activation
  - Modulation of transcription factors, nuclear receptors & gene expression
  - Modulation of inflammatory response
  - Antioxidant action
  - Cell cycle regulation
  - Competition with endogenous substrates for receptors
  - Modulation
  - Other….

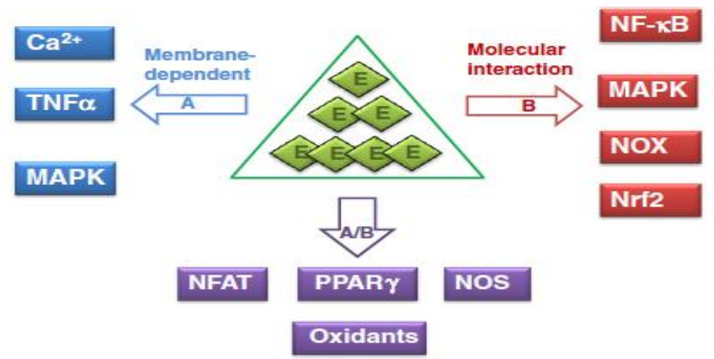
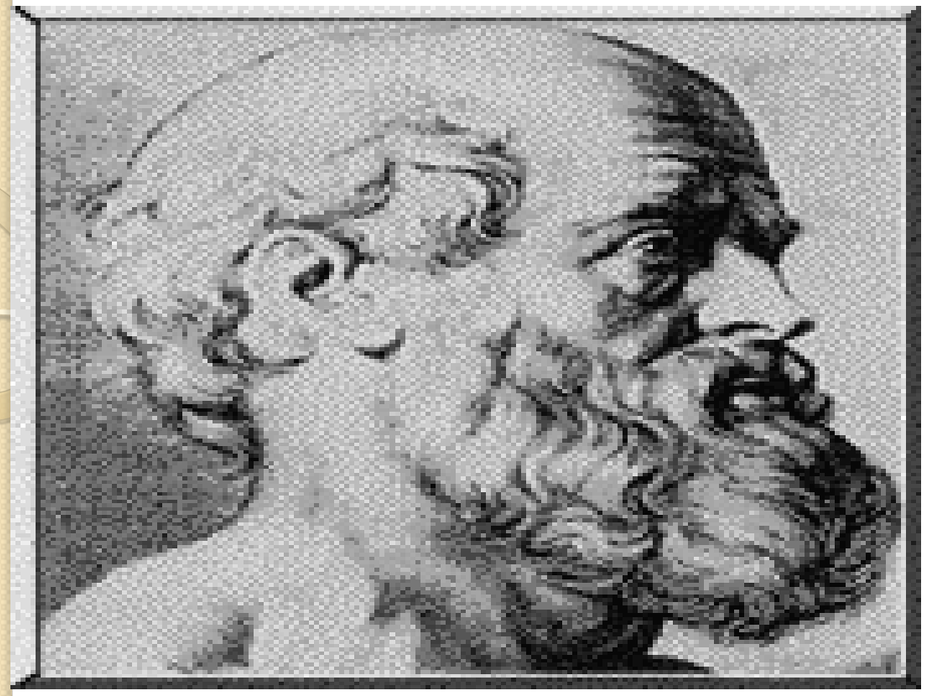
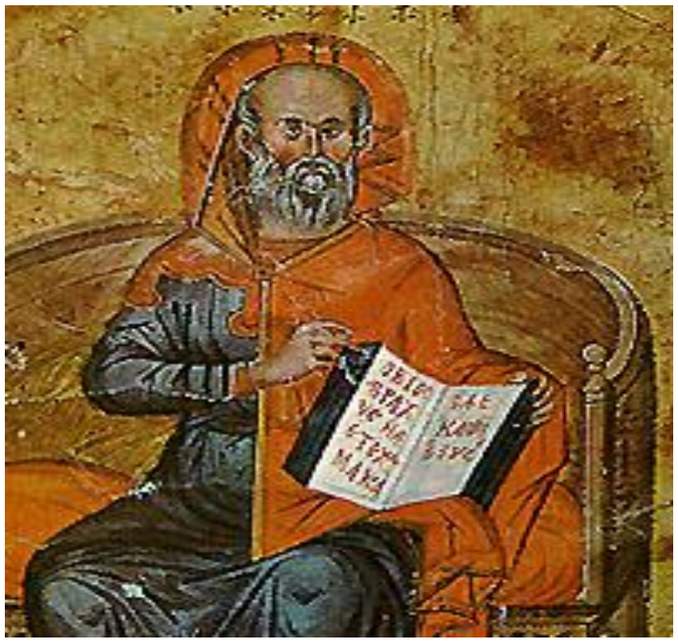


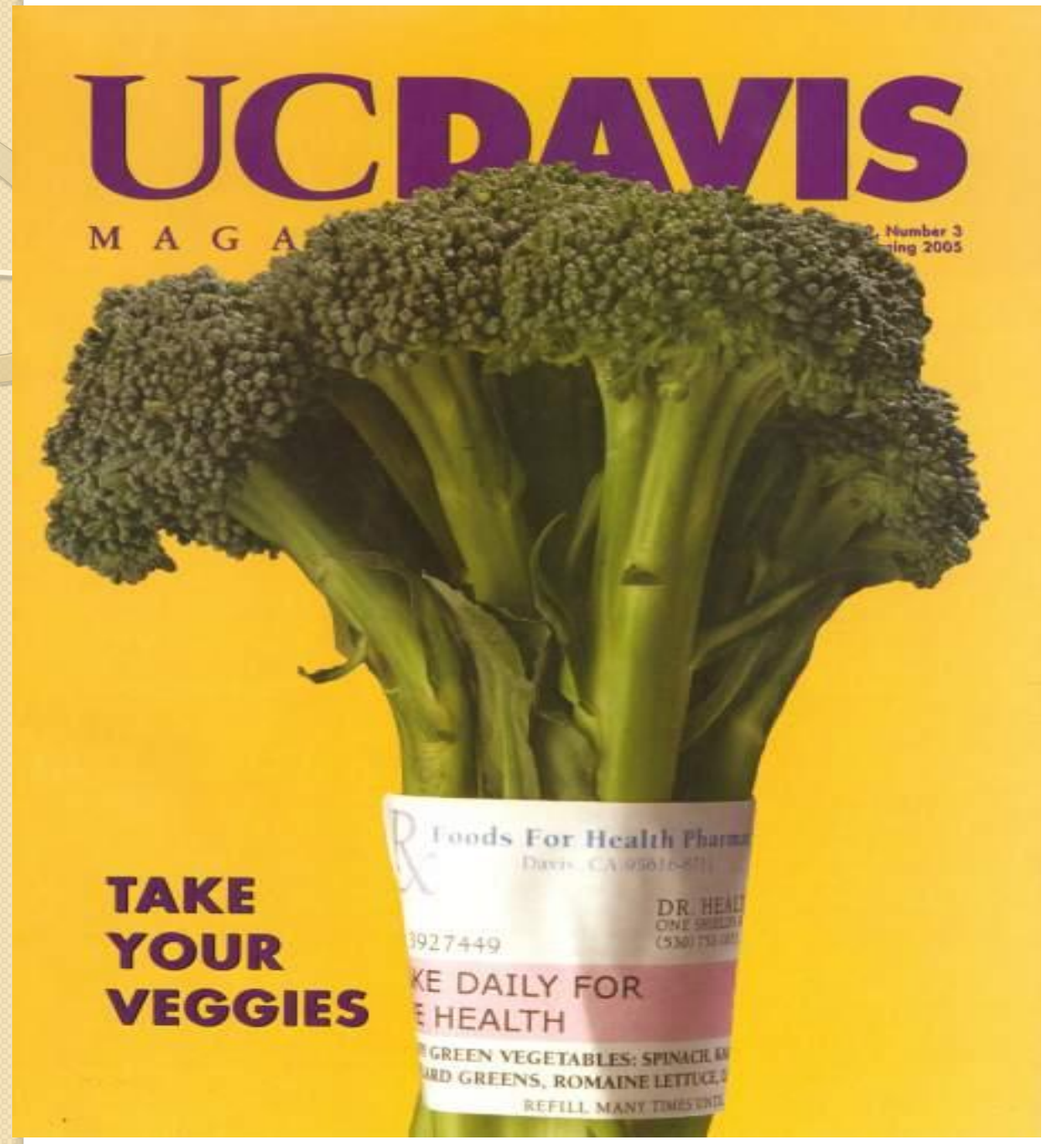
Fig. 6. Schematic summary of the potential actions of (−)-epicatechin and related procyanidins on various signaling pathways.



“Let food be thy medicine and medicine be thy food”

Hippocrates
The Father of Medicine
460 BC – 377 BC





- The public is embracing the concept of --“food as medicine” in response to the evolving health care crisis that is occurring in most developed countries.

- The goal of “optimal health” is desired by many, but the promise of the “optimal diet” and “miracle” or “super foods” is often more attractive than the recommendation of a balanced diet rich in fruits, vegetables and plant foods.

- How to achieve higher fruit & vegetable intakes; what is effective for

Dietary Patterns --

Examples of diet patterns rich in food phytochemicals…number of F/V servings is ≥ typical USDA dietary guidelines or the American Heart Association recommendations:

- DASH diet
- Mediterranean diet

DASH Diet
Dietary Approaches to Stop Hypertension

Control American Diet (37% total fat, 3.6 serv F/V, 2.5 serv meat, 0.4 serv dairy)

Fruit/Vegetable Diet (37% total fat, 8.5 serv F/V, 2.5 serv meat, 0.3 serv dairy, 0.6 serv nuts)

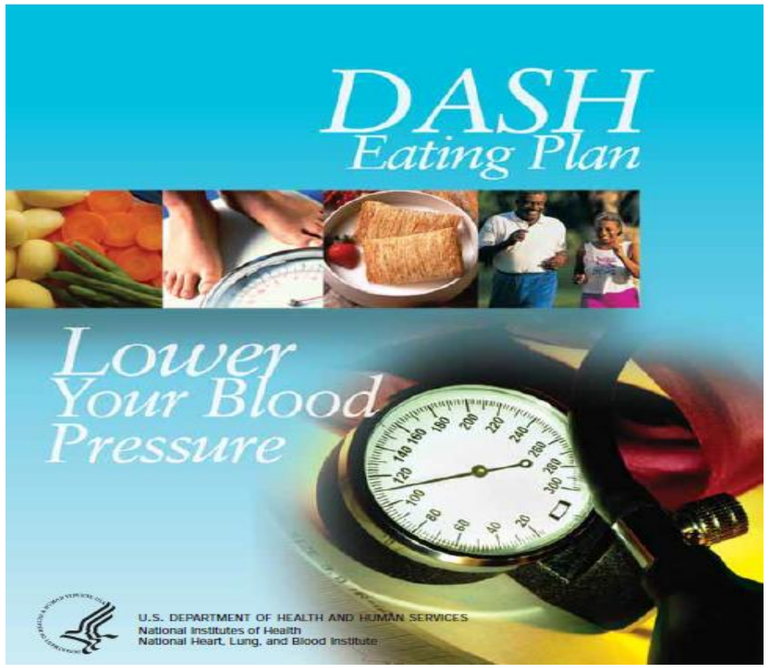
DASH Diet (27% total fat, 9.6 serv F/V, 1.6 serv meat, 2 serv low fat dairy, 0.7 serv nuts)

Outcomes:

- **Change in Blood Pressure: ↓ 5.5 mm HG systolic, 3.0 mm Hg diastolic on the Dash diet, intermediate results on F/V diet**

YOUR GUIDE TO

Lowering Your Blood Pressure With DASH



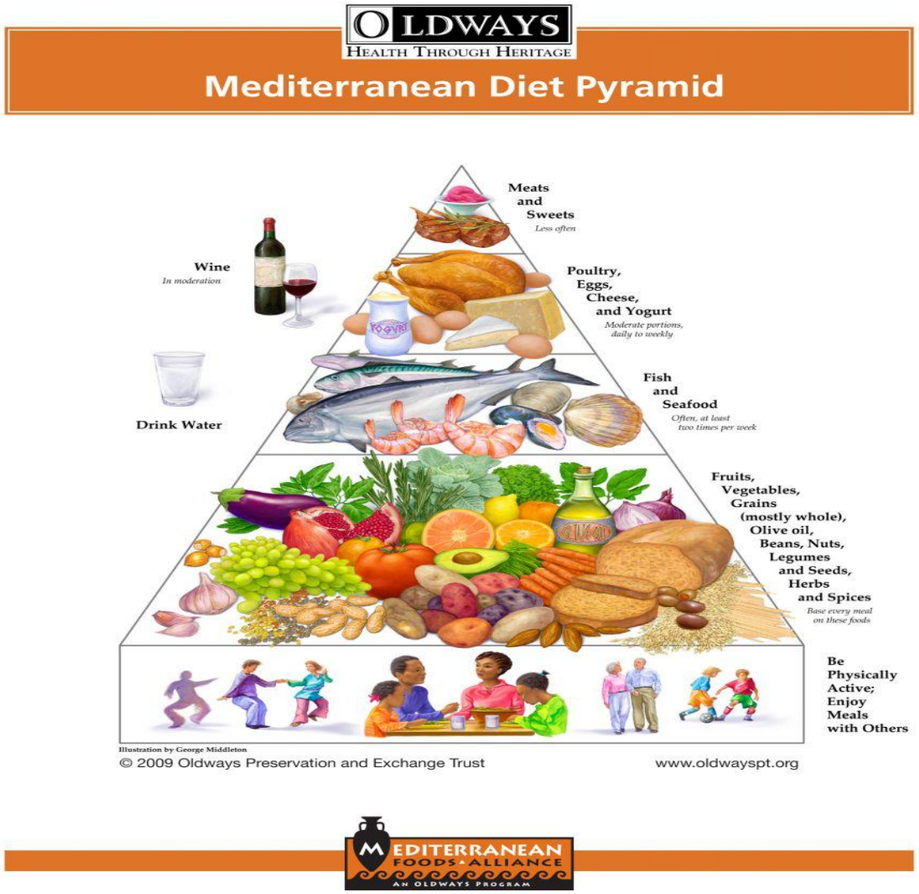
BOX 3

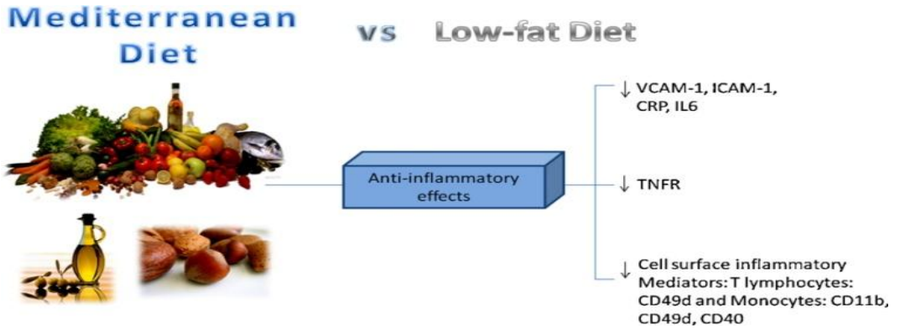
Following the DASH Eating Plan

Food Group	Daily Servings	Serving Sizes
Grains*	6–8	1 slice bread 1 oz dry cereal† ½ cup cooked rice, pasta, or cereal
Vegetables	4–5	1 cup raw leafy vegetable ½ cup cut-up raw or cooked vegetable ½ cup vegetable juice
Fruits	4–5	1 medium fruit ¼ cup dried fruit ½ cup fresh, frozen, or canned fruit ½ cup fruit juice
Fat-free or low-fat milk and milk products	2–3	1 cup milk or yogurt 1½ oz cheese
Lean meats, poultry, and fish	6 or less	1 oz cooked meats, poultry, or fish 1 egg†
Nuts, seeds, and legumes	4–5 per week	⅓ cup or 1½ oz nuts 2 Tbsp peanut butter 2 Tbsp or ½ oz seeds ½ cup cooked legumes (dry beans and peas)
Fats and oils§	2–3	1 tsp soft margarine 1 tsp vegetable oil 1 Tbsp mayonnaise 2 Tbsp salad dressing
Sweets and added sugars	5 or less per week	1 Tbsp sugar 1 Tbsp jelly or jam ½ cup sorbet, gelatin 1 cup lemonade

* *Whole grains are recommended for most grain servings as a good source of fiber and nutrients.*

† *Serving sizes vary between ½ cup and 1¼ cups, depending on cereal type. Check the product's Nutrition Facts label.*





Examples from PREDIMED Trial

Prevencion con Dieta Mediterranea

Large (n=7,447) multicenter European trial of individuals with risk factors but free of CVD. 3 diet arms Med+VOO, Med+nuts, Low fat. Followed multiple years

- Decreased cellular & circulating inflammatory biomarkers related to cardiovascular risk (Med diet vs Low fat diet) *2012 Pharamcol Res*
- Beneficial changes in apolipoproteins B, A-1 and their ratio (Med diet vs Low fat diet) *2011 Atherosclerosis*
- Reduced diabetes incidence (up to 52% ↓). After 4 yr follow-up, incidence of T2DM was 10.1% vs 17.9% (Med diet vs Low fat). *2011 Diabetes Care*

Predictors and Barriers of Fruit & Vegetable Intake

- Predictors
  - Favorable taste preferences
  - F > M
  - ↑ Age
  - ↑ SES
  - ↑ Educational status attained

- Barriers
  - Cost
  - Limited access
  - Time to prepare foods
  - Unfamiliarity with certain foods

Conclusions

- Scientific evidence supports chronic disease risk reduction related to F/V consumption, in some but not all conditions
- Health benefits of F/V appear to be associated with food phytochemicals, such as polyphenolic flavonoids, in addition to traditional nutrients
- Flavonoids are absorbed, metabolized & reach target tissues
- Mechanisms of biologic action for flavonoids are multifactorial & involve cellular events
- Benefits are seen with intake levels for F/V higher than USDA recommendations, and as part of a healthful diet pattern
- Average intake of F/V is low and has not changed much over last 20 years. Significant challenges exist regarding the goal of increasing