# Berries and Cardiovascular Health

Britt Burton-Freeman, PhD
Institute for Food Safety and Health
Illinois Institute of Technology
bburton@iit.edu

Berry Health Benefits Symposium
Westlake Village CA, 2011

# Speakers

- Marva Sweeny – Univ Prince Edward Island
*A hyperberry for hypertension*

- Indika Edirisinghe – Illinois Institute of Technology
*Effect of fruit antioxidant on endothelial function*

- Arpita Basu – Oklahoma State University
*Berries and Metabolic Syndrome*

- Charles Coulliard – Laval University, Canada
*Evidence Supporting the cardiometabolic effects of cranberries*

# OUTLINE

- **Cardiovascular Disease – what is it?**
- **Statistics**
- **Risk factors**
  - Traditional
  - Emerging
- **Managing risk through diet and lifestyle**
- **Research**

# Cardiovascular disease
## What is it?

**Class of diseases that include the heart and blood vessels**

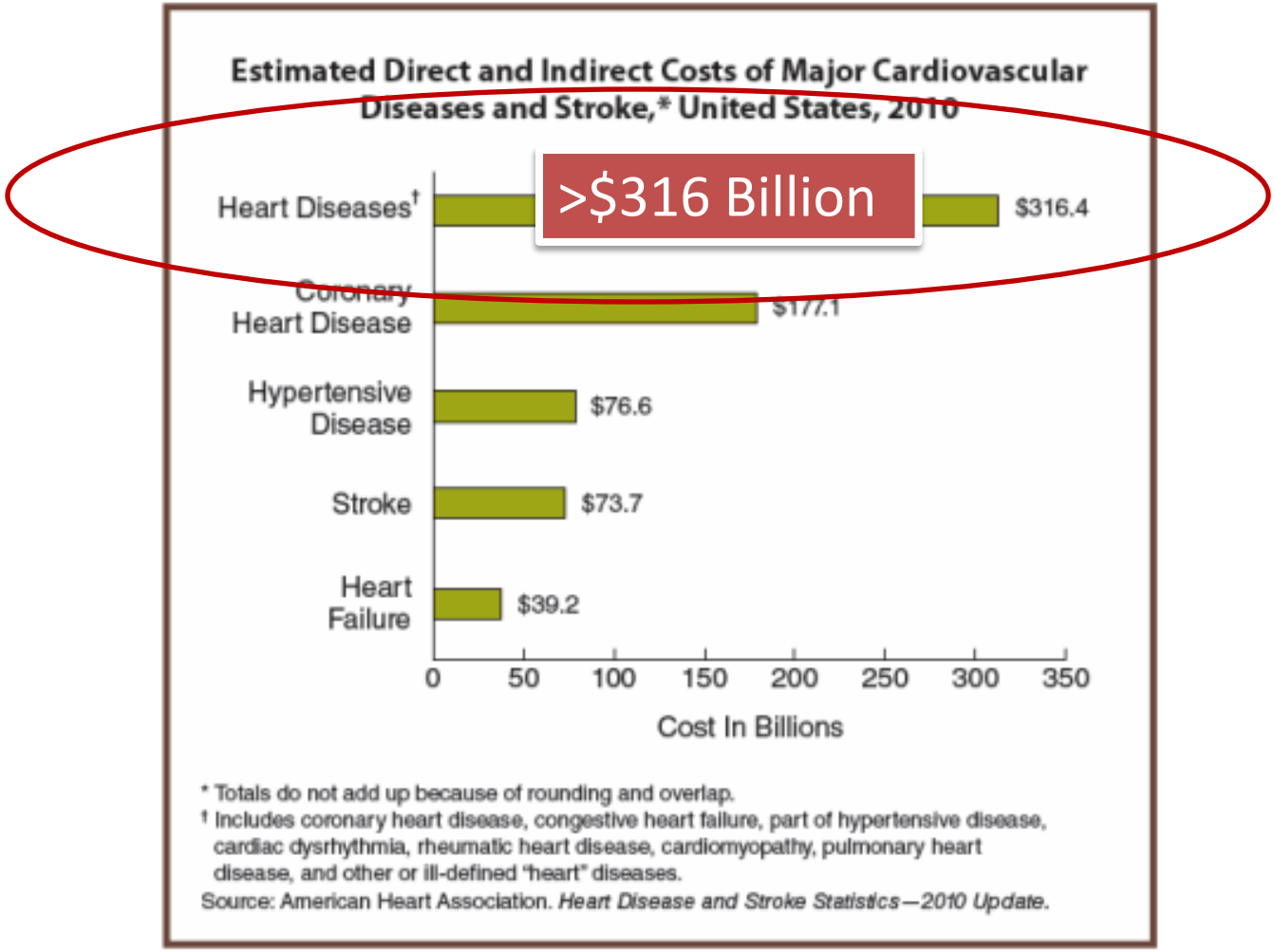
- Coronary Heart Disease
- Atherosclerosis
- Stroke
- Peripheral artery disease
- Heart Failure
- Hypertension
- Congenital Heart Defects

# Death from Cardiovascular Disease still the #1 killer among men and women in the U.S.

- Accounts for 34.2% of all deaths (>800,000 d/yr)
- 2400 Americans die from CVD each day
- 1 person every 37 seconds

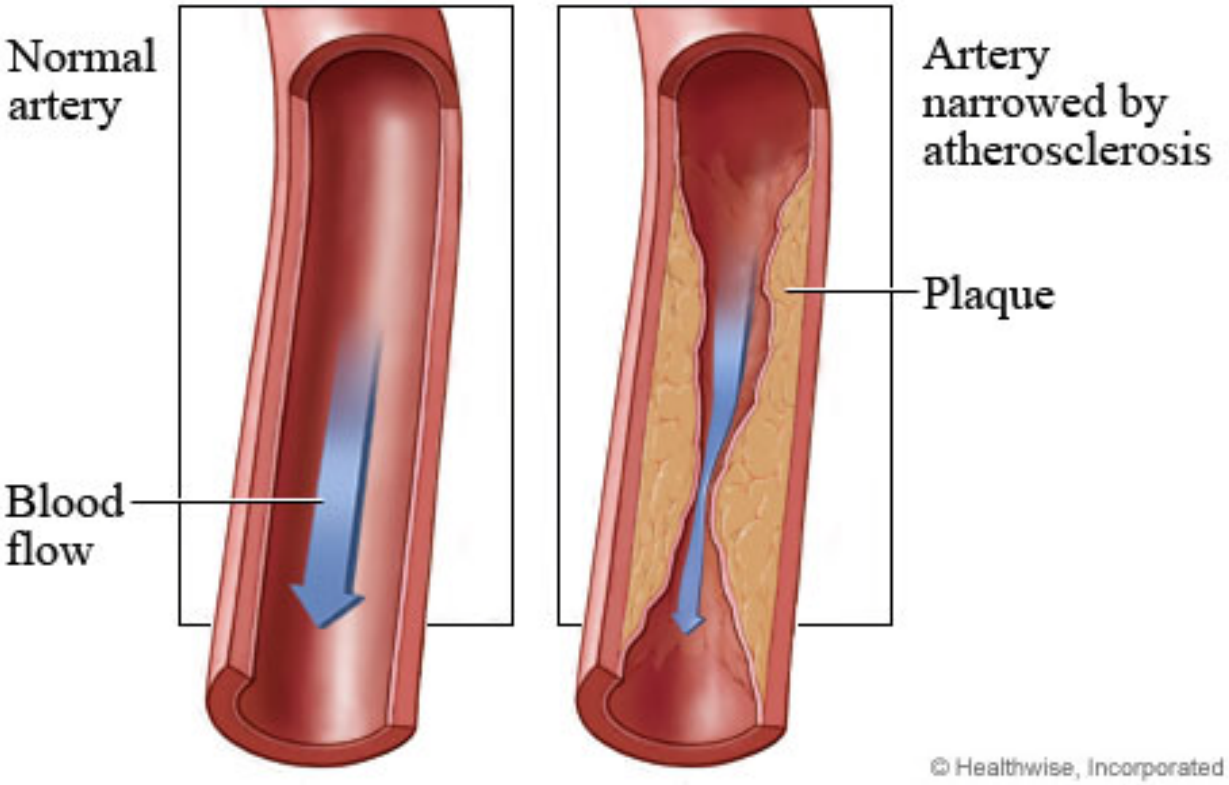
**Heart Disease and Stroke Stats, Circulation 2009**

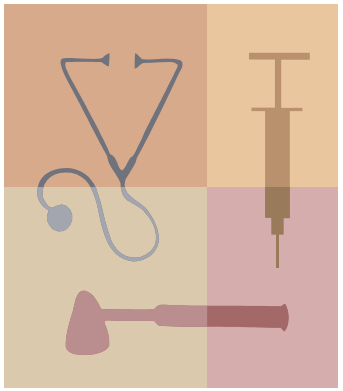
# Costs of Cardiovascular Disease, 2010




CDC: http://www.cdc.gov/chronicdisease/resources/publications/AAG/dhdsp.htm#aag

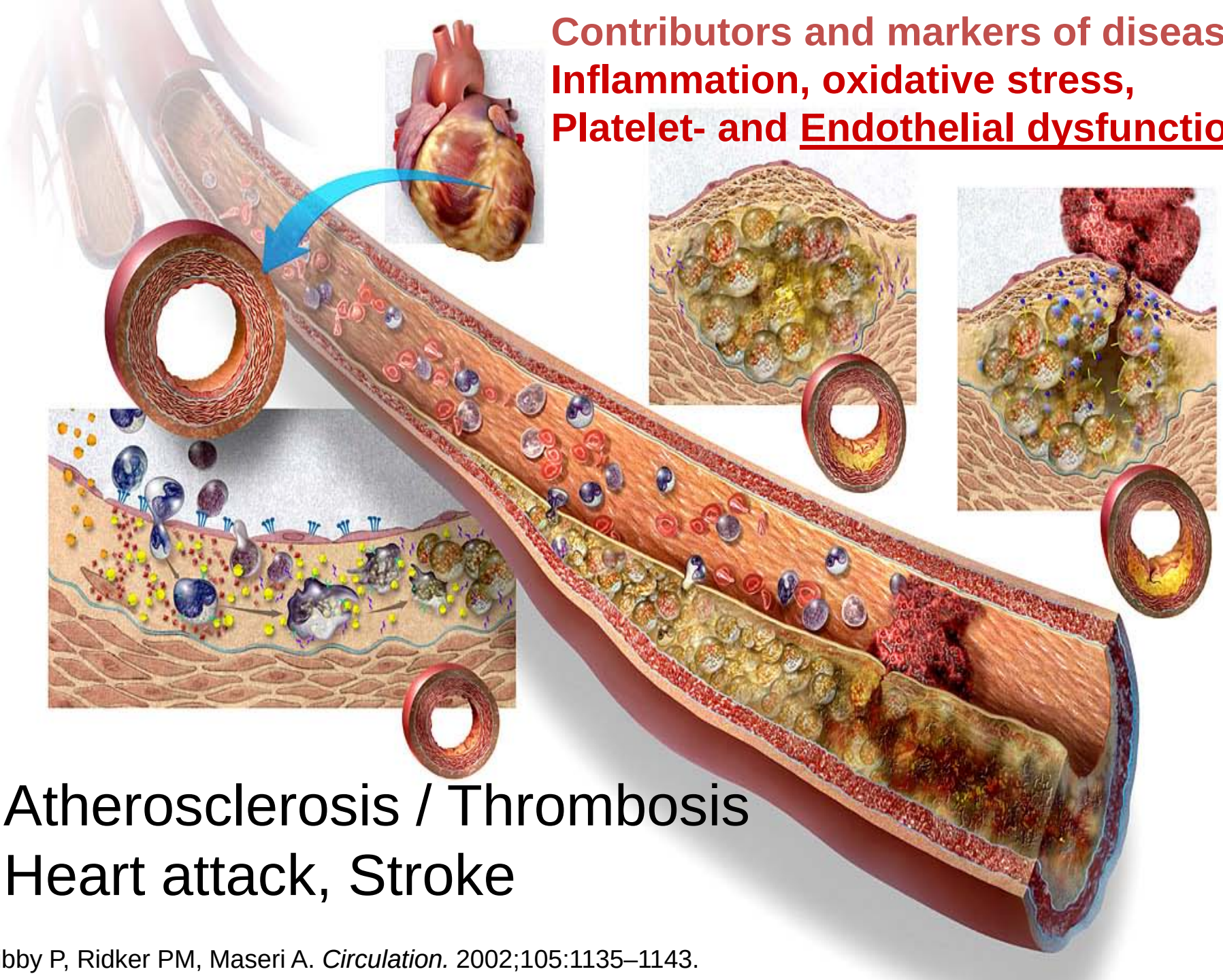
# CVD/CAD is no longer considered just a cholesterol accumulation disease



Lipid panel
Family history
Medical history
Lifestyle history

## Contributors and markers of disease:
## Inflammation, oxidative stress, Platelet- and Endothelial dysfunction



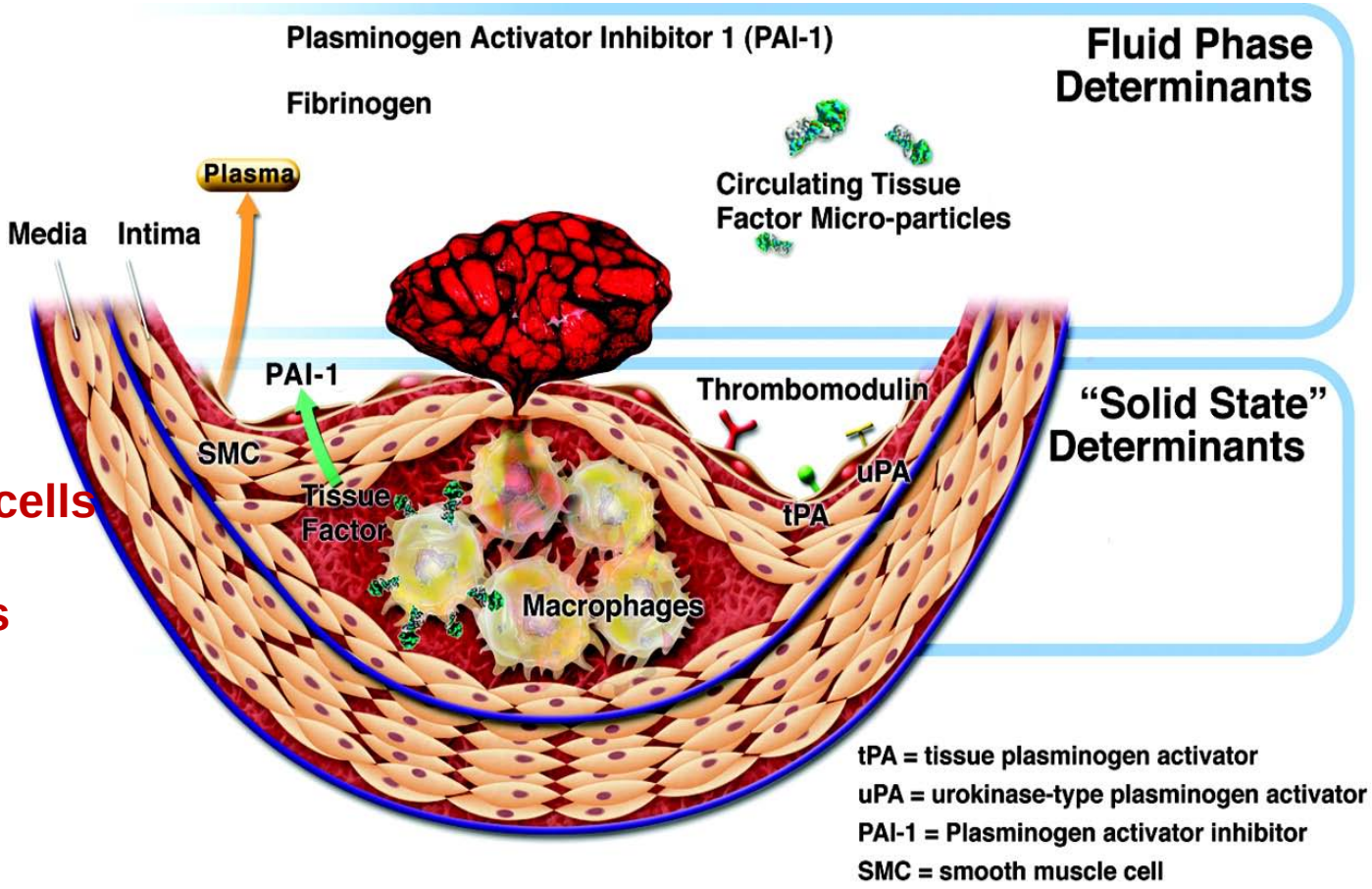
Atherosclerosis / Thrombosis
Heart attack, Stroke

Libby P, Ridker PM, Maseri A. *Circulation.* 2002;105:1135–1143.

# Atheromas contain multiple cell types that critically influence atherogenesis

**Vascular cells**
**--Endothelium**
**--Smooth muscle cells**

**Inflammatory cells**
**--Macrophages**
**--T lymphocytes**
**--Mast cells**




Libby, P. et al. Circulation 2005;111:3481-3488

American Heart Association®
Learn and Live℠

# Traditional Risk Factors for Cardiovascular Disease

- Smoking
- High blood pressure
- Dyslipidemia
- Overweight, Obesity
- Diabetes
- Inactivity
- Diet
- Stress
- Age
- Gender
- Family history/ genetics
- Race

Modifiable

Endothelial Dysfunction

# Selected Emerging Risk Factors and Biomarkers

**Lipids**

- Lp(a)
- apoA/apoB
- Particle size/density

**Inflammation**

- CRP
- SAA
- IL-6
- IL-18
- TNF
- Adhesion mols
- Lp-$PLA_2$
- CD40L
- CSF

**Hemostasis/Thrombosis**

- Homocysteine
- tPA/PAI-1
- TAFI
- Fibrinogen
- D-dimer

**Oxidation**

- Ox-LDL
- Glutathione
- MPO

**Genetic**

- Asp299Gly polymorphism in TLR4 gene
- MCP-1 2578G allele
- CX3CR1 chemokine receptor polymorphism V249I
- 16Gly variant of $\beta_2$-adrenergic receptor
- 260T/T CD14 allele
- 117 Thr/Thr variant of CSF
- LIGHT

CSF = colony-stimulating factor

MPO = myeloperoxidase

TAFI = thrombin activatable fibrinolysis inhibitor

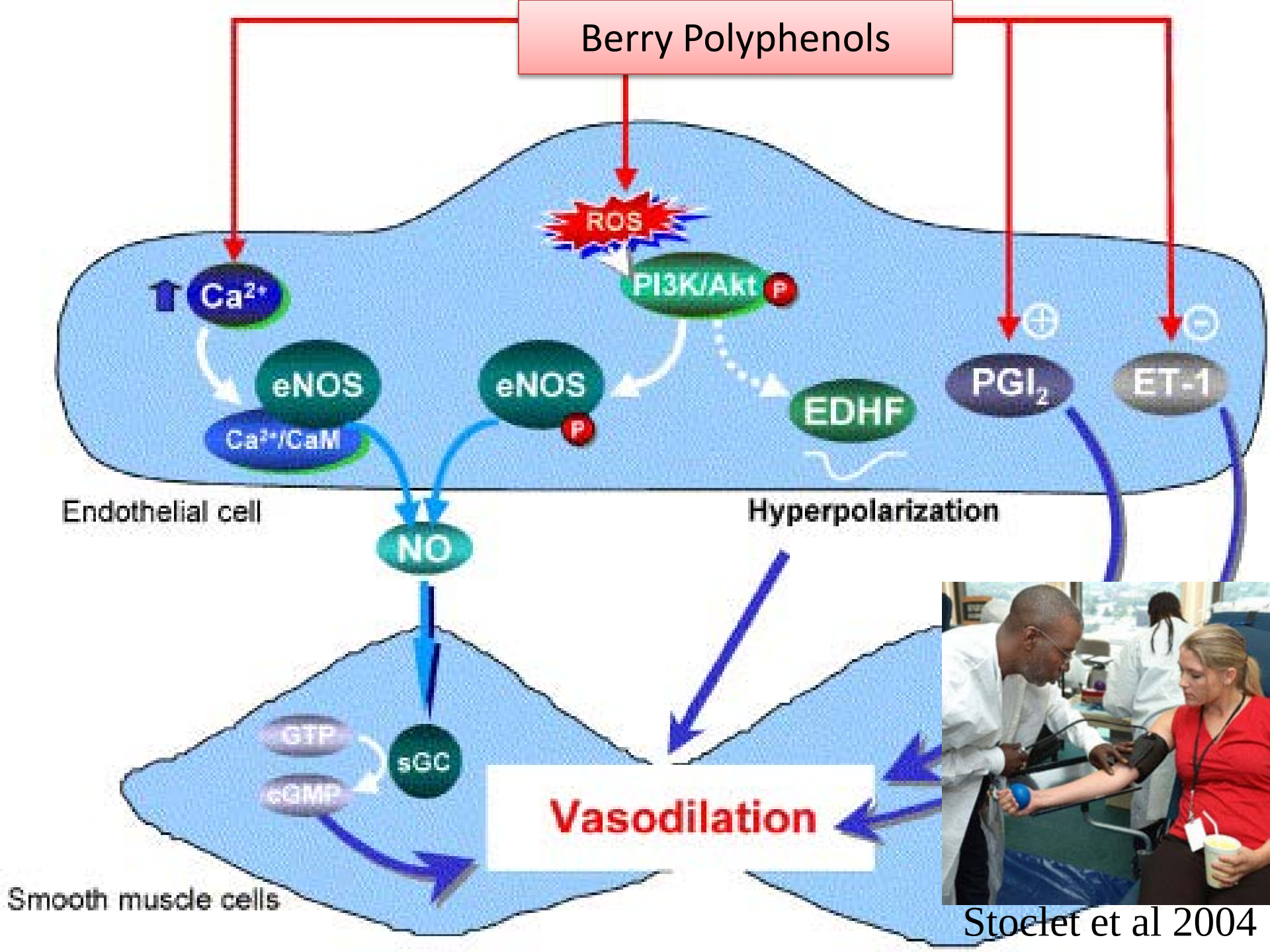
Adapted from Stampfer MJ et al. *Circulation*. 2004;109(suppl):IV3-IV5.

# Risk Factors for Cardiovascular Disease

## Directly Influenced by Diet

- Smoking
- High blood pressure
- High Cholesterol -Total cholesterol, LDL
- High Triglycerides
- Overweight and Obesity
- Diabetes (Type II)
- Insulin resistance
- Oxidative stress
- Blood properties
- Dietary factors
  - Food choice, preparation, portion, etc.
- Inactivity
- Stress

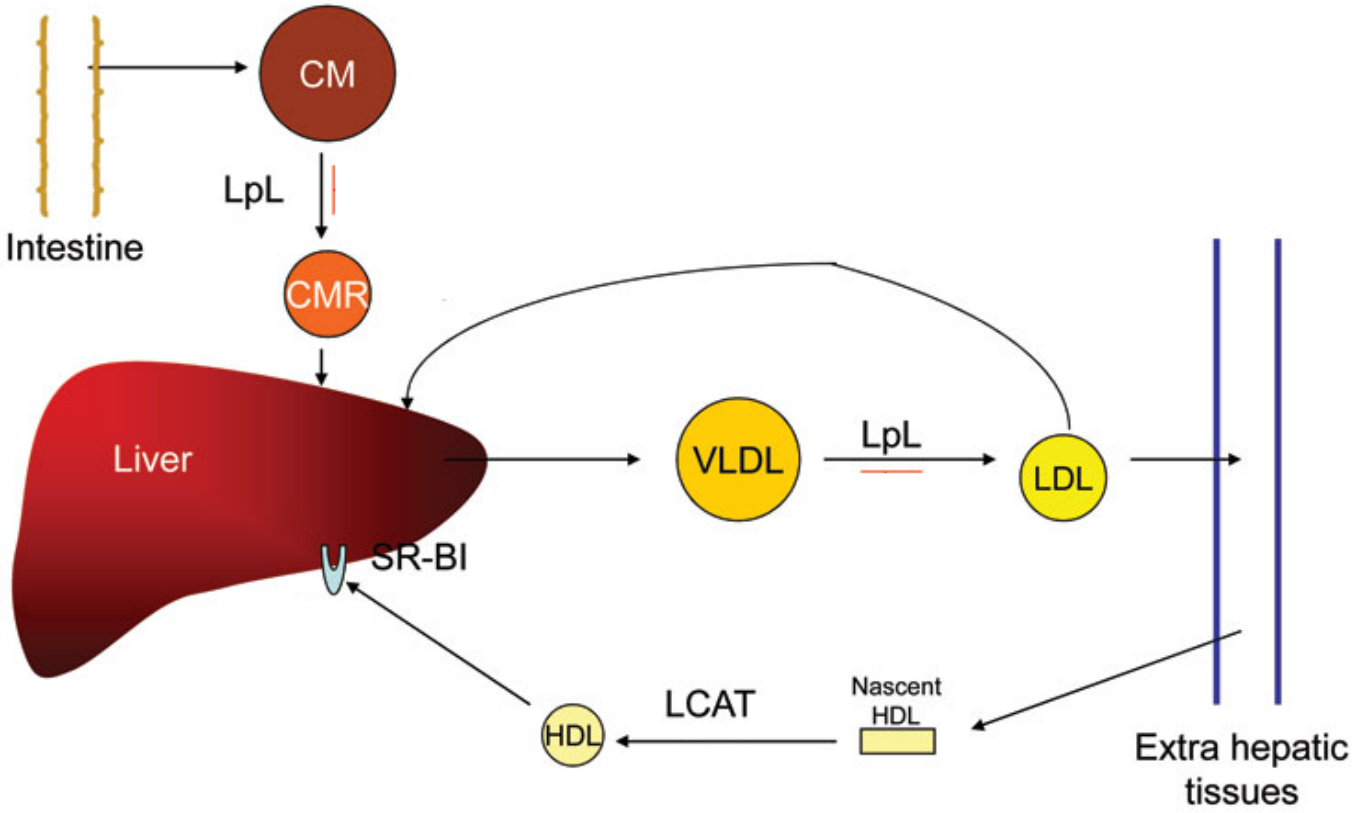
Berries ?




Stoclet et al 2004

# Blood Lipids / lipoprotein metabolism influenced by diet

## Fat type, Berries?



# Selected Emerging Risk Factors and Biomarkers

**Lipids**

- Lp(a)
- apoA/apoB
- Particle size/density

**Inflammation**

- CRP
- SAA
- IL-6
- IL-18
- TNF
- Adhesion mols
- Lp-PLA$_2$
- CD40L
- CSF

**Hemostasis/Thrombosis**

- Homocysteine
- tPA/PAI-1
- TAFI
- Fibrinogen
- D-dimer

**Oxidation**

- Ox-LDL
- Glutathione
- MPO

**Genetic**

- Asp299Gly polymorphism in TLR4 gene
- MCP-1 2578G allele
- CX3CR1 chemokine receptor polymorphism V249I
- 16Gly variant of $\beta_2$-adrenergic receptor
- 260T/T CD14 allele
- 117 Thr/Thr variant of CSF
- LIGHT

CSF = colony-stimulating factor

MPO = myeloperoxidase

TAFI = thrombin activatable fibrinolysis inhibitor

Adapted from Stampfer MJ et al. *Circulation*. 2004;109(suppl):IV3-IV5.

# Strawberry Intake and Elevations in Lipids and C-Reactive Protein

**Table 4.** Relative Risks (RRs) and 95% Confidence Intervals of Having Elevations in Various Lipid Parameters and C-Reactive Protein according to Categories of Strawberry Intake in a Cross-Sectional Study among 26,965 Women

| | Category of Strawberry Intake | | | | |
|---|---|---|---|---|---|
| | None (n = 6,743) | 1–3 servings/month (n = 11,498) | 1 serving/week (n = 6,693) | ≥2 servings/week (n = 2,032) | P, trend* |
| Total Cholesterol ≥240 mg/dL | 22.5† | 21.7 | 22.2 | 22.1 | |
| Age-, treatment-adjusted RR‡ | 1.00 (ref) | 0.95 (0.88–1.02) | 0.95 (0.88–1.03) | 0.95 (0.84–1.07) | 0.58 |
| Multivariate-adjusted RR§ | 1.00 (ref) | 1.02 (0.94–1.11) | 0.99 (0.90–1.10) | 0.96 (0.82–1.13) | 0.50 |
| LDL Cholesterol ≥160 mg/dL | 14.6 | 13.3 | 14.2 | 13.9 | |
| Age-, treatment-adjusted RR‡ | 1.00 (ref) | 0.89 (0.81–0.97) | 0.93 (0.84–1.03) | 0.91 (0.78–1.05) | 0.53 |
| Multivariate-adjusted RR§ | 1.00 (ref) | 0.95 (0.86–1.04) | 0.98 (0.87–1.10) | 0.91 (0.75–1.09) | 0.41 |
| HDL Cholesterol ≥60 mg/dL | 29.0 | 30.8 | 29.5 | 28.4 | |
| Age-, treatment-adjusted RR‡ | 1.00 (ref) | 1.11 (1.04–1.19) | 1.06 (0.98–1.14) | 1.02 (0.91–1.14) | 0.61 |
| Multivariate-adjusted RR§ | 1.00 (ref) | 1.02 (0.94–1.11) | 0.97 (0.88–1.06) | 0.95 (0.82–1.10) | 0.39 |
| Non-HDL Cholesterol ≥190 mg/dL | 20.7 | 19.1 | 19.7 | 19.4 | |
| Age-, treatment-adjusted RR‡ | 1.00 (ref) | 0.89 (0.83–0.96) | 0.89 (0.82–0.98) | 0.88 (0.77–1.00) | 0.17 |
| Multivariate-adjusted RR§ | 1.00 (ref) | 0.99 (0.90–1.08) | 0.96 (0.86–1.07) | 0.89 (0.75–1.05) | 0.18 |
| TC/HDL Ratio ≥6 units | 10.9 | 9.2 | 9.6 | 10.3 | |
| Age-, treatment-adjusted RR‡ | 1.00 (ref) | 0.80 (0.90–1.07) | 0.96 (0.86–1.06) | 0.89 (0.75–1.05) | 0.48 |
| Multivariate-adjusted RR§ | 1.00 (ref) | 0.96 (0.85–1.07) | 0.96 (0.83–1.11) | 1.02 (0.83–1.27) | 0.60 |
| C-reactive protein ≥3 mg/L | 37.2 | 36.6 | 37.6 | 36.7 | |
| Age-, treatment-adjusted RR‡ | 1.00 (ref) | 0.96 (0.90–1.02) | 0.98 (0.91–1.05) | 0.94 (0.84–1.04) | 0.35 |
| Multivariate-adjusted RR§ | 1.00 (ref) | 1.03 (0.95–1.11) | 0.99 (0.90–1.09) | 0.86 (0.75–0.99) | 0.012 |

* Test for trend based on ordinal variable containing median value for each quintile.

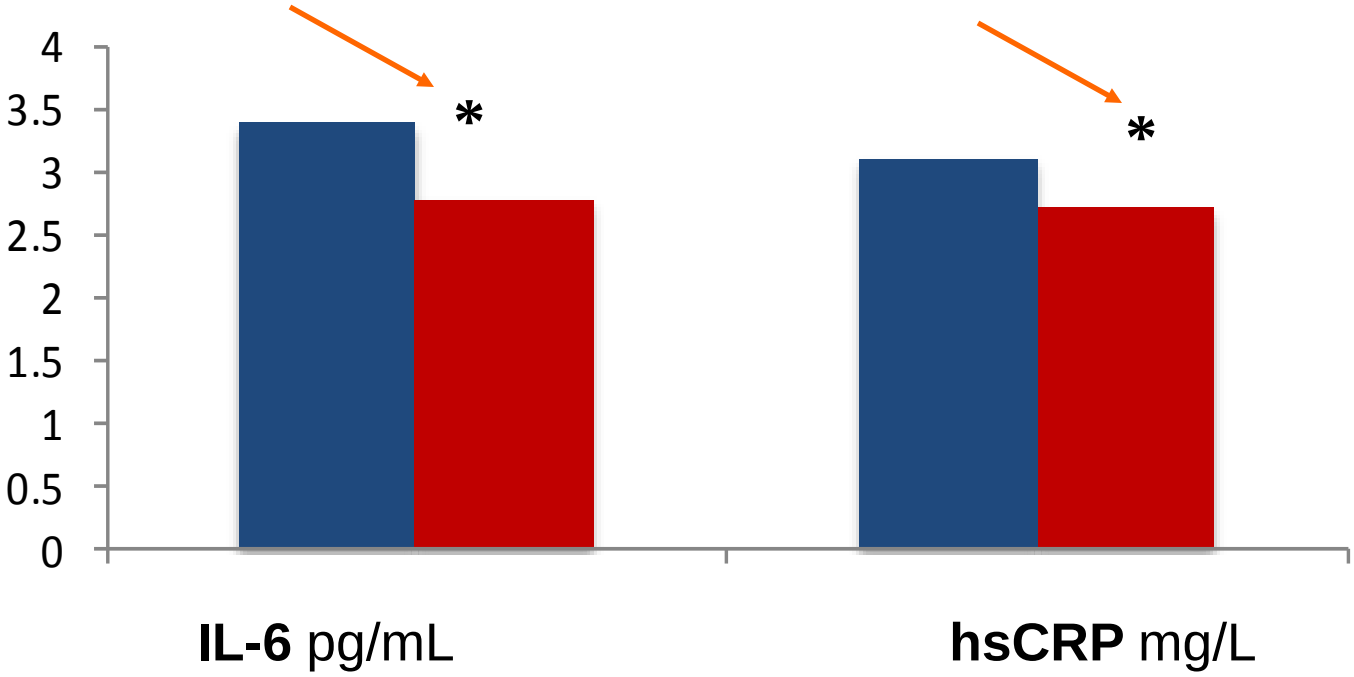
† Percent of women with elevations in each lipid parameter and C-reactive protein.

‡ Adjusted for age, randomized aspirin treatment, randomized vitamin E treatment, randomized beta-carotene treatment, and total energy intake.

§ Adjusted for the covariates above plus lifestyle, clinical and dietary factors: body mass index, exercise, alcohol intake, smoking, post-menopausal hormone use, parental history of myocardial infarction <60 years, hypertension, hypercholesterolemia, diabetes, and the intake of fruits and vegetables, fiber, folate, vitamin C, potassium, saturated fat, and total flavonoids.

**Sesso HD *et al*. J Am Coll Nutr 2006;26:303-310**

# Strawberry reduces inflammatory response to a meal in overweight (OW) men and women




Placebo + 40% fat Meal

Strawberry + 40% fat Meal

*Edirisinghe et al. BJN 2011*

# Selected Emerging Risk Factors and Biomarkers

**Lipids**

- Lp(a)
- apoA/apoB
- Particle size/density

**Inflammation**

- CRP
- SAA
- IL-6
- IL-18
- TNF
- Adhesion mols
- Lp-$PLA_2$
- CD40L
- CSF

**Hemostasis/Thrombosis**

- Homocysteine
- tPA/PAI-1
- TAFI
- Fibrinogen
- D-dimer

**Oxidation**

- Ox-LDL
- Glutathione
- MPO

**Genetic**

- Asp299Gly polymorphism in TLR4 gene
- MCP-1 2578G allele
- CX3CR1 chemokine receptor polymorphism V249I
- 16Gly variant of $\beta_2$-adrenergic receptor
- 260T/T CD14 allele
- 117 Thr/Thr variant of CSF
- LIGHT

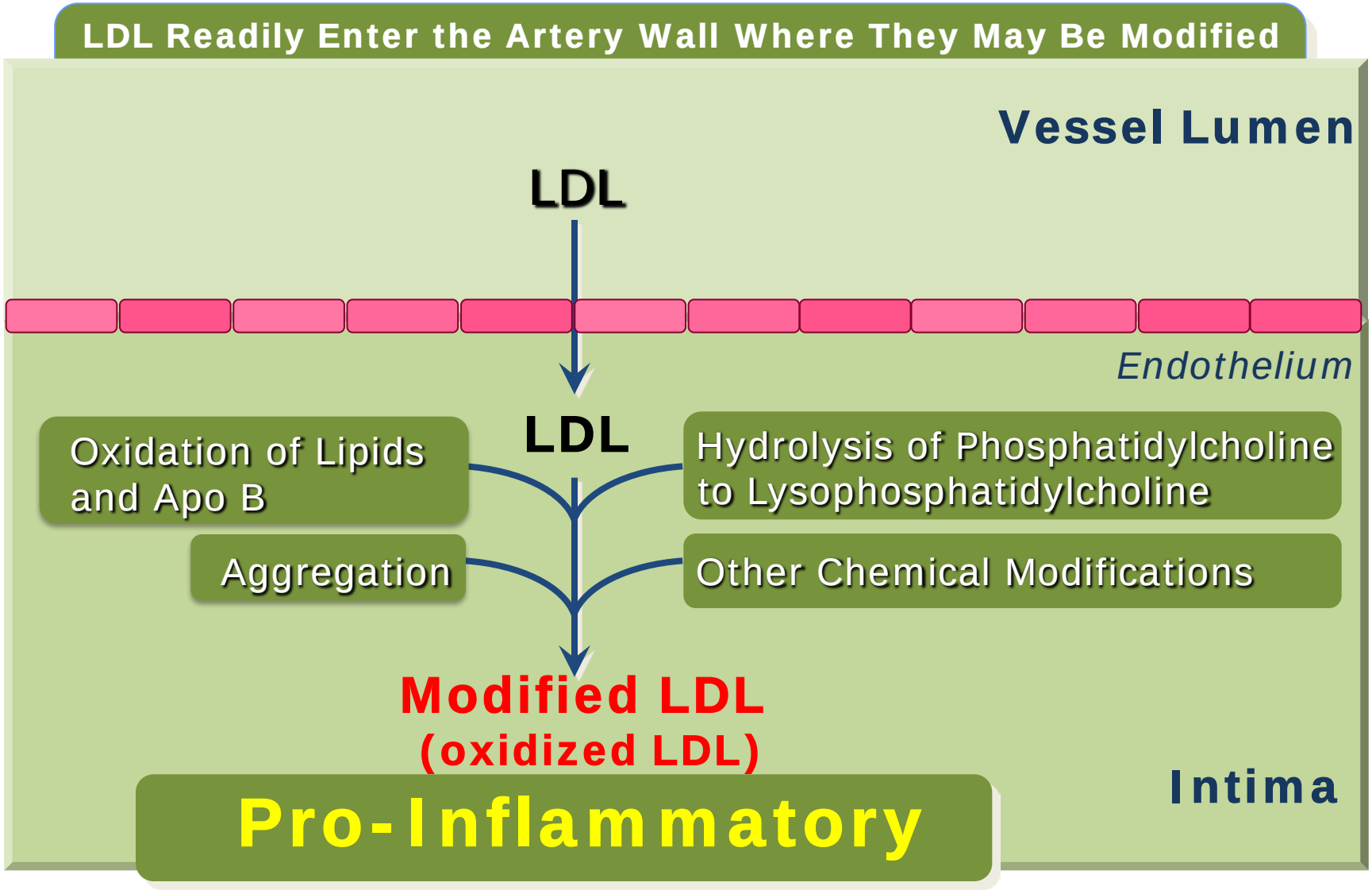
CSF = colony-stimulating factor

MPO = myeloperoxidase

TAFI = thrombin activatable fibrinolysis inhibitor

Adapted from Stampfer MJ et al. *Circulation*. 2004;109(suppl):IV3-IV5.

# Modified / Oxidized LDL



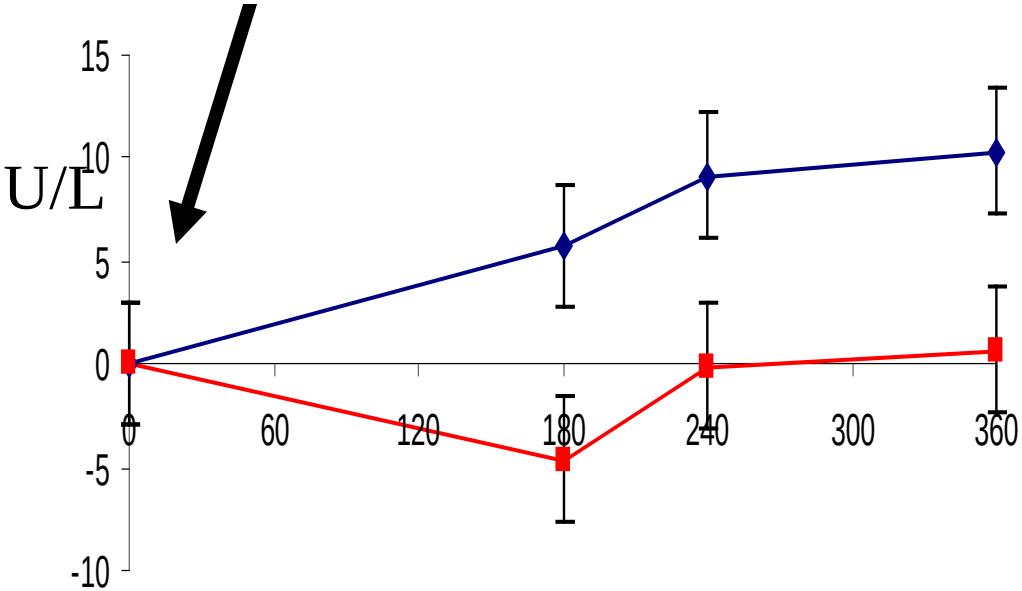

Steinberg D, et al. *N Engl J Med.* 1989;320:915-924.

Slide Source: Lipids Online

# Strawberry prevents meal-induced increase in oxidized LDL in OW men and women


Breakfast + Placebo beverage

Breakfast + Strawberry beverage




**Oxidation**

**Protection**

Treatment, p<0.0008
Time, p=NS

*Burton-Freeman et al. JACN 2010*

# Selected Emerging Risk Factors and Biomarkers

**Lipids**

- Lp(a)
- apoA/apoB
- Particle size/density

**Inflammation**

- CRP
- SAA
- IL-6
- IL-18
- TNF
- Adhesion mols
- Lp-$PLA_2$
- CD40L
- CSF

**Hemostasis/Thrombosis**

- Homocysteine
- tPA/PAI-1
- TAFI
- Fibrinogen
- D-dimer

**Oxidation**

- Ox-LDL
- Glutathione
- MPO

**Genetic**

- Asp299Gly polymorphism in TLR4 gene
- MCP-1 2578G allele
- CX3CR1 chemokine receptor polymorphism V249I
- 16Gly variant of $\beta_2$-adrenergic receptor
- 260T/T CD14 allele
- 117 Thr/Thr variant of CSF
- LIGHT

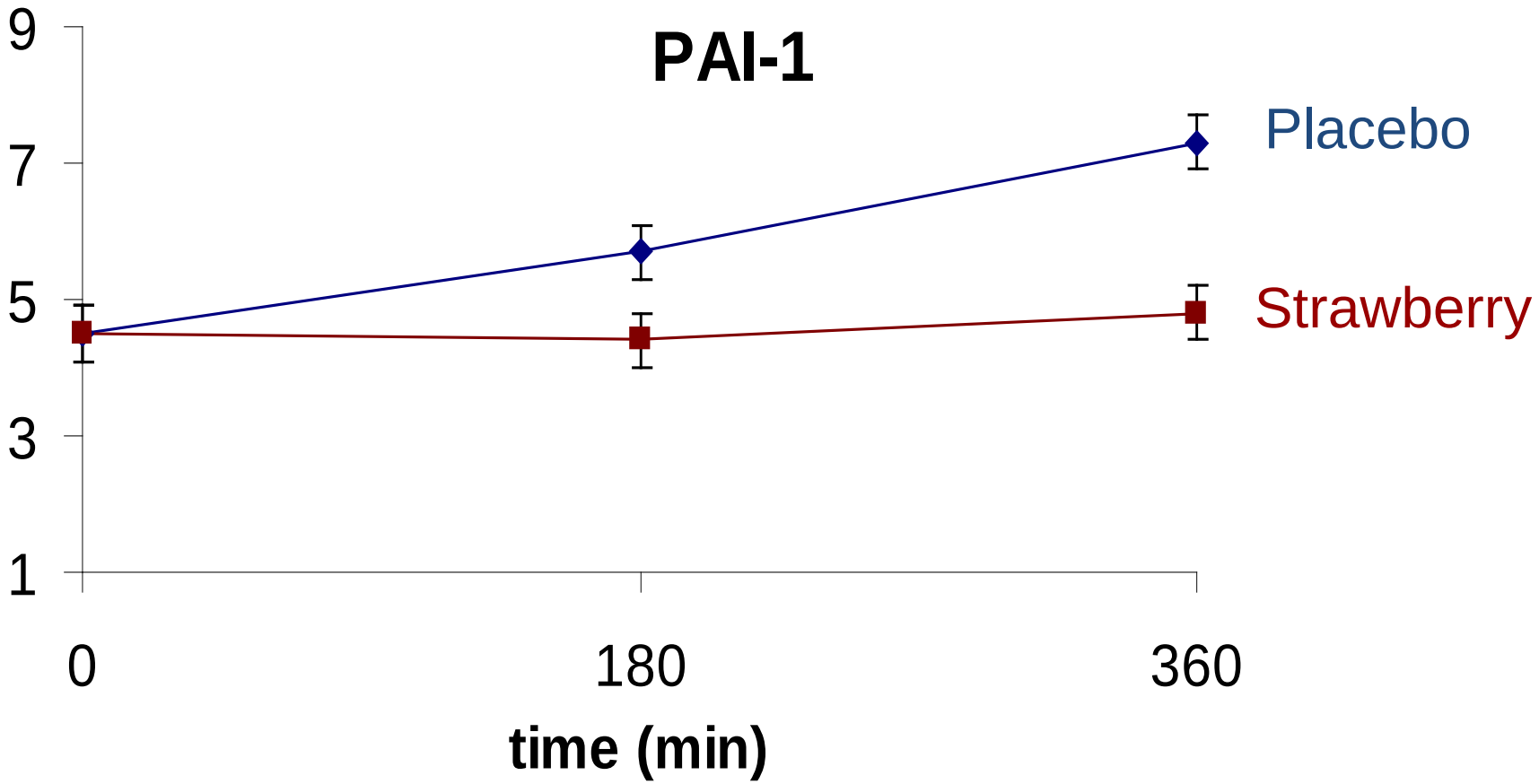
CSF = colony-stimulating factor

MPO = myeloperoxidase

TAFI = thrombin activatable fibrinolysis inhibitor

Adapted from Stampfer MJ et al. *Circulation*. 2004;109(suppl):IV3-IV5.

# 6-weeks on strawberry supplemented diet protects against meal-induced increases in PAI-1.




*Ellis et al. 2011 J Athero Thrombosis*

# Berry Intake and CVD Summary

- Complex disease
  - Multiple targets for promoting health
- Berries appear to have role in reducing CVD risk
- Several unanswered questions, but promising opportunity
- Future research warranted