Berries and Cardiovascular Health

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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
Costs of Cardiovascular Disease, 2010

Estimated Direct and Indirect Costs of Major Cardiovascular Diseases and Stroke, * United States, 2010

- Heart Diseases*: $316.4 Billion
  - Coronary Heart Disease: $177.1 Billion
  - Hypertensive Disease: $76.6 Billion
  - Stroke: $73.7 Billion
  - Heart Failure: $39.2 Billion

* Totals do not add up because of rounding and overlap.
† Includes coronary heart disease, congestive heart failure, part of hypertensive disease, cardiac dysrhythmia, rheumatic heart disease, cardiomyopathy, pulmonary heart disease, and other or ill-defined “heart” diseases.

Source: American Heart Association, Heart Disease and Stroke Statistics—2010 Update.

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

Atheromas contain multiple cell types that critically influence atherogenesis.

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

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

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

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**CSF** = colony-stimulating factor

**MPO** = myeloperoxidase  
**TAFI** = thrombin activatable fibrinolysis inhibitor

Adapted from Stampfer MJ et al.  
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
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
- IL-6
- TNF
- Lp-PLA2
- CD40L
- CSF
- SAA
- IL-18
- Adhesion mols

### Oxidation
- Ox-LDL
- MPO

### Hemostasis/Thrombosis
- Homocysteine
- tPA/PAI-1
- TAFI
- D-dimer
- Fibrinogen

### Genetic
- Asp299Gly polymorphism in TLR4 gene
- MCP-1 2578G allele
- CX3CR1 chemokine receptor polymorphism V249I
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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

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

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

**IL-6 pg/mL**

**Placebo + 40% fat Meal**

**Strawberry + 40% fat Meal**

**hsCRP mg/L**

*Edirisinghe et al. BJN 2011*
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Modified / Oxidized LDL

LDL Readily Enter the Artery Wall Where They May Be Modified

Vessel Lumen

Endothelium

LDL

Oxidation of Lipids and Apo B
Aggregation

Hydrolysis of Phosphatidylcholine to Lysophosphatidylcholine
Other Chemical Modifications

Modified LDL (oxidized LDL)

Pro-Inflammatory


Slide Source: Lipids Online
Strawberry prevents meal-induced increase in oxidized LDL in OW men and women

Breakfast + Placebo beverage
Breakfast + Strawberry beverage

Treatment, p<0.0008
Time, p=NS

Burton-Freeman et al. JACN 2010
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| Inflammation | CRP | SAA          |
|              | IL-6 | IL-18       |
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6-weeks on strawberry supplemented diet protects against meal-induced increases in PAI-1.
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