Bioactive food components in global public health

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University of Southampton

World Cancer Research Fund International
BIOACTIVE COMPOUNDS AND CHRONIC DISEASE

- Burden of chronic disease
- Nutritional aspects
- Evolutionary aspects
- Issues and Uncertainties
- Proposed principles
BIOACTIVE COMPOUNDS AND CHRONIC DISEASE

• Burden of chronic disease
• Nutritional aspects
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CAUSE SPECIFIC MORTALITY
ENGLAND 2000

MALE

CVD 40%
OTHER 20%
ACCIDENTS 2%
RESPIRATORY 10%
CANCER 28%

FEMALE

CVD 40%
OTHER 24%
ACCIDENTS 2%
RESPIRATORY 11%
CANCER 24%

Dept of Health, 2000
MAJOR CAUSES OF DEATH
USA 2002

- CHD: 29%
- Cancer: 23%
- Other: 29%
- Accidents: 4%
- Stroke: 7%
- Diabetes: 3%
- Respiratory: 5%

NCHS 2005
GLOBAL DISTRIBUTION OF CAUSES OF DEATHS

WHO, 2003
BIOACTIVE COMPOUNDS AND CHRONIC DISEASE

- Burden of chronic disease
- **Nutritional aspects**
- Evolutionary aspects
- Issues and Uncertainties
- Proposed principles
Nutrition and chronic disease

- Cardiovascular diseases
- Cancer
- Bone health
- Obesity
- Diabetes
Nutrition and chronic disease

- Cardiovascular diseases
- Cancer
- Bone health
- Obesity
- Diabetes
CHD Mortality and Serum Cholesterol

MRFIT n=356222
Deaths per 1000

Decile mmol/L

Serum cholesterol mmol/L

1 2 3 4 5 6 7 8 9 10
4.0 4.5 4.8 5.1 5.4 5.6 5.8 6.1 6.6 7.5
Dietary Fatty Acids and Total Serum Cholesterol

Change in total serum cholesterol (mmol/L) per 1% energy change in kcal from fat

Modified from Grundy et al 1981
CHANGE IN LDL-CHOLESTEROL WITH PLANT STEROLS OR STANOLS

From: Law 2000
Prevalence of High Blood Pressure in Americans by Age and Sex
NHANES: 1999-2002

Source: CDC/NCHS and NHLBI.
Estimated 10-Year Stroke Risk in 55-Year-Old Adults According to Levels of Various Risk Factors - Framingham Heart Study

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
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</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td>95-105</td>
<td>130-148</td>
<td>130-148</td>
<td>130-148</td>
<td>130-148</td>
<td>130-148</td>
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<tr>
<td>Diabetes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Cigarettes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Prior Atrial Fib.</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Prior CVD</td>
<td>No</td>
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</table>

Estimated 10-Year CHD Risk in 55-Year-Old Adults According to Levels of Various Risk Factors
Framingham Heart Study

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure (mm Hg)</td>
<td>120/80</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
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<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>200</td>
<td>240</td>
<td>240</td>
<td>240</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>50</td>
<td>50</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Diabetes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cigarettes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

mm Hg = millimeters of mercury
mg/dL = milligrams per deciliter of blood

The Dietary Approaches to Stop Hypertension (DASH) trial

Sacks et al, 2001

Sacks et al, 2001
Vegetable intake and Relative Risk of CHD Mortality in Men

Adjusted for age and energy, carotenoids, vitamins E and C intakes

Knekt et al, 1994
VITAMINS: MAJOR VASCULAR EVENTS

<table>
<thead>
<tr>
<th>Vascular event</th>
<th>VITAMINS (10269)</th>
<th>PLACEBO (10267)</th>
<th>Rate ratio &amp; 95% CI</th>
<th>VITAMINS better</th>
<th>PLACEBO better</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major coronary</td>
<td>1063</td>
<td>1047</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Any stroke</td>
<td>511</td>
<td>518</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revascularisation</td>
<td>1058</td>
<td>1086</td>
<td></td>
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<tr>
<td>ANY OF ABOVE</td>
<td>2306 (22.5%)</td>
<td>2312 (22.5%)</td>
<td>0% SE 3 reduction</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Vitamins = 600 mg E, 250 mg C and 20 mg beta-carotene

Heart Protection Study 2002
Homocysteine and CHD Observational Studies

Degree of adjustment

+++ +++ +++ +++

++++ +++ ++ ++

+++++++ +++ ++ +

+++++++ ++ + +

+++++++ + + + +

+++++++ + + + +

Relative Risk

1.3 (1.1-1.5)
1.6 (1.4-1.7)
1.9 (1.6-2.3)
PHYTOESTROGENS AND CARDIOVASCULAR DISEASE

van der Schouw et al 2005
EPIC: Colorectal cancer risk

RR

1,10

1,00

0,90

0,80

0,70

0,60

1 2 3 4 5

quintiles of exposure

Fruits
Fruits + Veg
Vegetable

Statistical models adjusted by height, weight, physical activity, energy intake, smoking

B. de Mesquita, E.Riboli, P.Ferrari et al., IARC, 2002, in press
Relative risk of colorectal cancer by quintile of fibre intake, with and without adjustment for energy

S. Bingham et al., IARC, 2002
VITAMINS: SITE-SPECIFIC CANCER INCIDENCE

<table>
<thead>
<tr>
<th>Condition</th>
<th>VITAMINS (10269)</th>
<th>PLACEBO (10267)</th>
<th>Rate ratio &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>228</td>
<td>223</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>181</td>
<td>165</td>
<td></td>
</tr>
<tr>
<td>Connective tissue</td>
<td>60</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>247</td>
<td>284</td>
<td></td>
</tr>
<tr>
<td>Central nervous system</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Haematological</td>
<td>58</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>42</td>
<td>43</td>
<td></td>
</tr>
</tbody>
</table>

ANY CANCER (except non melanoma skin): 800 (7.8%) and 817 (8.0%) with a 2% SE 5 reduction (NS)

Non-melanoma skin: 217 and 228

Heart Protection Study, 2002
Chronic disease - nutritional perspective

- Human nutrition - Demand-led process; supply to meet physiological demand for function (metabolism, mechanical work)
- Demand depends on genetic background, lifetime experience, and current environment
- Human metabolism evolved through natural selection
- Natural selection operates through reproductive inheritance
Chronic disease - nutritional perspective

• Nutrient - component of metabolic pathways (or precursor) found in food/drink

• Essential nutrients - essential components of metabolism expected in the environment - biosynthetic pathways not preserved

• “Non-essential” nutrients - essential components of metabolism whose biosynthetic pathways must be preserved
Bioactive compounds - nutritional perspective

- Are they nutrients?
- Are they essential?
- Is there a physiological demand?
Bioactive compounds - nutritional perspective

• Are they nutrients? NO
• Are they essential?
• Is there a physiological demand?
Bioactive compounds
- nutritional perspective

• Are they nutrients? NO

• Are they essential? NO

• Is there a physiological demand?
Bioactive compounds - nutritional perspective

- Are they nutrients? NO
- Are they essential? NO
- Is there a physiological demand? NO
Bioactive compounds - nutritional perspective

- Are they nutrients? NO
- Are they essential? NO
- Is there a physiological demand? NO
- So does their supply influence metabolism and health and if so how?
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QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.
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Bioactive compounds - evolutionary perspective

- Post-reproductive events largely irrelevant to natural selection
- Post-reproductive effects of environmental exposures cannot be predicted on evolutionary basis
- Bioactive compounds do not meet evolutionarily determined metabolic demand
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Bioactive food components

- Amount and form consumed
- Absorption - effects if not absorbed
- Metabolism
- Systemic, tissue, intracellular distribution
- Effects of metabolites
  - Biochemistry of etiologic pathway
  - Validated markers of risk?
  - Effects in vitro, in animal model
  - Effects in human in vivo
- Interactions
- Biological effects vs health effects
Foods and chronic disease

- Food components vs whole diets
  - Interactions
  - Confounding
    - Food, diet, behaviour
  - Dose
  - Formulation
  - Study design
Foods and chronic disease

• Evidence issues
  – Simple vs complex models and interventions
  – Timing of intervention
  – Duration of intervention

• Type of evidence
  – Trial vs observational
  – Prospective vs retrospective
  – Laboratory vs clinical

• Complexity of foods/diets/lifestyle
  – Confounding - cause/effect
  – Interactions
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BIOACTIVE COMPOUNDS AND CHRONIC DISEASE

• Foods and diets associate with chronic disease risk
• Foods and diets are complex and associate with other behaviors
• Many food components have biological activity
• Some bioactive components may have health promoting potential
• Some bioactive components may have adverse effects
BIOACTIVE COMPOUNDS AND CHRONIC DISEASE

• Does this potential translate to reality?
• How to test this?
• What paradigm to use?
Bioactive food components

- Epidemiology - associations
- Physiology - absorption, metabolism, distribution and utilisation
- Lab - potential efficacy/safety
- “Omics” - human biology
- Clinical - human health
  - Dose/form
  - Population studied
  - Timing of intervention
  - Duration of intervention
  - Outcomes - intermediate or health
    - beneficial or adverse
BIOACTIVE COMPOUNDS AND CHRONIC DISEASE

• Bioactive food components are incidental to nutrition
• Food components can have adverse and positive effects
• Studies need to address effectiveness in prevention and treatment - hard end points
• Better elucidation of the etiologic pathway and the effects of bioactive components is key to designing informative clinical studies
• Effects on validated determinants of risk need to be demonstrated
• Research on food components is important
BIOACTIVE COMPOUNDS AND CHRONIC DISEASE

• For global public health population-wide interventions are needed
• Interventions must have demonstrated high benefit to risk ratio
• Varying exposures beyond usual experience needs to demonstrate both safety and efficacy
• Unusual interventions (single component, non-nutrient, high dose) are not meeting nutritional demand and a pharmacologic paradigm is appropriate at present
• Current public health strategies should be food based