Is Eating More Fruits and Vegetables Really Important to Health Promotion?

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Jean Mayer USDA Human Nutrition Research Center on Aging
Friedman School of Nutrition Science and Policy
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F&V Reduce the Risk of Cerebrovascular and Cardiovascular Disease

F&V Intake is Associated with Reduced Mortality from Ischemic Heart Disease
European Prospective Investigation into Cancer and Nutrition (EPIC) – Heart Study

F&V Intake and Type 2 Diabetes
A Meta-analysis

F&V Intake and Cancer Risk:
An Early Consensus

It is concluded that consumption of higher levels of vegetables and fruit is associated consistently, although not universally, with a reduced risk of cancer at most sites.

The association is most marked for epithelial cancers - particularly those of the alimentary and respiratory tracts - and, currently, is weak to nonexistent for hormone-related cancers.

The association exists for a wide variety of vegetables and fruit with some suggestion that raw forms are associated most consistently with lower risk.
F&V Reduce Risk of Cancer: 28 Prospective Cohort Meta-analysis

+ 100 g fruit/d  
+ 100 g veg/d

Reduced risk

Colon stomach bladder lung breast


F&V Intake and Cancer Risk: Nutrients and Mechanisms of Action

A large number of potentially anticarcinogenic agents are found in F&V, including carotenoids, vitamins C and E, selenium, dietary fiber, dihydrotachysterol, glucosinolates and indoles, isothiocyanates, flavonoids, phenols, protease inhibitors, plant sterols, allium compounds, and limonene.

These agents have both complementary and overlapping mechanisms of action, including the induction of detoxification enzymes, inhibition of nitrosamine formation, provision of substrate for formation of antineoplastic agents, dilution and binding of carcinogens in the digestive tract, alteration of hormone metabolism, antioxidant effects, and others.

It appears extremely unlikely that any one substance is responsible for all the associations seen.

Steinmetz and Potter. Cancer Causes Control 1991

F&V Intake and Cancer Risk: The Early Hypothesis

Humans are adapted to a high intake of plant foods that supply substances crucial to the maintenance of the organism, but only some of which are currently called 'essential nutrients.' Cancer may be the result of reducing the level of intake of foods that are metabolically necessary - it may be a disease of maladaptation.

Steinmetz and Potter. Cancer Causes Control 1991

World Cancer Research Fund
American Institute for Cancer Research
Expert Reports

1997 - There is 'convincing' evidence that high intakes of F&V decrease the risk for cancers of the mouth and pharynx, esophagus, stomach, colorectum and lung.

Produce for Better Health Foundation
Blue-Purple “Health Claims”*

• A lower risk of some cancers
• Urinary tract health
• Memory function
• Healthy aging

* as part of a low-fat diet
Produce for Better Health Foundation

**Yellow-Orange “Health Claims”**

- Heart health
- Vision health
- A healthy immune system
- A lower risk of some cancers

* as part of a low-fat diet

**Red “Health Claims”**

- Heart health
- Memory function
- A lower risk of some cancers
- Urinary tract health

* as part of a low-fat diet

**Green “Health Claims”**

- A lower risk of some cancers
- Vision health
- Strong bones and teeth

* as part of a low-fat diet

**White “Health Claims”**

- Heart health
- Cholesterol levels that are already healthy
- A lower risk of some cancers

* as part of a low-fat diet

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**Achievement of Daily Vegetable Consumption Target**

[Graph showing the percentage of population achieving the vegetable consumption target in average day]

NDP Group. Nutrient Intake Database. 2010

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**Achievement of Daily Fruit Consumption Target**

[Graph showing the percentage of population achieving the fruit consumption target in average day]

NDP Group. Nutrient Intake Database. 2010
Average Daily Consumption of F&V

- NDP Group. Nutrient Intake Database. 2010

Percentage of Adults Consuming Fruit ≥2 Times Daily

- CDC MMWR 2010

Percentage of Adults Consuming Vegetables ≥3 Times Daily

- CDC MMWR 2010

Daily Consumption of F&V

- Only 6% of individuals achieve their recommended target for vegetables in an average day
- Only 8% of individuals achieve their recommended target for fruit in an average day
- Eight of the states with the lowest fruit and vegetable consumption are also in the top 10 states with the highest obesity rates

F&V Intake Reduce Risk for CVD But Not Cancer or Major Chronic Disease

- Prospective Cohorts
  - Nurses Health Study
  - Health Professionals Follow-up Study
  - n=109,635
  - 14 y f/u

F&V Intake and Oral/Pharyngeal Cancer Case Control Studies

- Vainio et al. Nutr Cancer 2006
Vegetable Consumption and Stomach Cancer

**Case Control Studies**

0.66 (0.61-0.71)

**Cohort Studies**

0.94 (0.84-1.06)

Vainio et al. Nutr Cancer 2006

Vegetable Consumption and Colorectal Cancer

**Case Control Studies**

0.63 (0.56-0.70)

**Cohort Studies**

0.97 (0.87-1.08)

Vainio et al. Nutr Cancer 2006

F&V Intake and Lung Cancer

**Case Control Studies**

Fruit Intake

0.70

0.45-1.07

0.77

0.71-0.84

Vegetable Intake

0.69

0.63-0.75

0.80

0.73-0.88

Vainio et al. Nutr Cancer 2006

World Cancer Research Fund

American Institute for Cancer Research

Expert Reports

1997 - There is 'convincing' evidence that high intakes of F&V decrease the risk for cancers of the mouth and pharynx, esophagus, stomach, colorectum and lung.

2007 - There is ‘probable’ or ‘limited-suggestive’ evidence that high intakes of F&V decrease the risk for cancers of the mouth and pharynx, esophagus, stomach, colorectum and lung.

Results from Large Prospective Cohort Studies: F&V and Colorectal Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Ca</th>
<th>RR - Fruit</th>
<th>RR - Veg</th>
<th>RR - F&amp;V</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPIC</td>
<td>2810</td>
<td>0.88</td>
<td>0.92</td>
<td>0.86</td>
</tr>
<tr>
<td>NIH-AARP (M)</td>
<td>2046</td>
<td>1.06</td>
<td>0.82</td>
<td>0.91</td>
</tr>
<tr>
<td>NIH-AARP (F)</td>
<td>924</td>
<td>1.09</td>
<td>1.12</td>
<td>1.08</td>
</tr>
<tr>
<td>Pooling Project</td>
<td>5838</td>
<td>0.93</td>
<td>0.94</td>
<td>0.91</td>
</tr>
</tbody>
</table>

Van Duijnhoven et al. Am J Clin Nutr 2009


Results from Large Prospective Cohort Studies: F&V and Lung Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Ca</th>
<th>RR - Fruit</th>
<th>RR - Veg</th>
<th>RR - F&amp;V</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPIC</td>
<td>1830</td>
<td>0.80</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>NIH-AARP (M)</td>
<td>3834</td>
<td>0.91</td>
<td>0.93</td>
<td>0.93</td>
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<tr>
<td>NIH-AARP (F)</td>
<td>2201</td>
<td>0.97</td>
<td>1.05</td>
<td>0.98</td>
</tr>
<tr>
<td>Pooling Project</td>
<td>3206</td>
<td>0.77</td>
<td>0.88</td>
<td>0.79</td>
</tr>
</tbody>
</table>

Büchner et al. Cancer Causes Control 2010


Results from Large Prospective Cohort Studies: F&V and All Cancers

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Ca</th>
<th>RR - Fruit</th>
<th>RR - Veg</th>
<th>RR - F&amp;V</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPIC</td>
<td>30,604</td>
<td>0.94</td>
<td>0.93</td>
<td>0.89</td>
</tr>
<tr>
<td>Japan PHCPS</td>
<td>3230</td>
<td>1.02</td>
<td>0.94</td>
<td>0.96</td>
</tr>
<tr>
<td>NIH-AARP (M)</td>
<td>35,071</td>
<td>0.98</td>
<td>0.94</td>
<td>--</td>
</tr>
<tr>
<td>NIH-AARP (F)</td>
<td>15,792</td>
<td>0.99</td>
<td>1.04</td>
<td>--</td>
</tr>
<tr>
<td>NHS/NPFS</td>
<td>9261</td>
<td>1.01</td>
<td>0.99</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Boffetta et al. J Natl Cancer Inst 2010
George et al. Am J Clin Nutr 2009
Hung et al. J Natl Cancer Inst 2004

Deaths Attributable to Total Effects of Modifiable Risk Factors by Disease

Deaths Attributable to Total Effects of Modifiable Risk Factors by Disease

Limitations and Sources of Error in Observational Studies

- Limited range of intake
- Poor precision of exposure measurement
- Dietary changes after single assessment
- Residual confounding
- Reverse causality
- Inability of statistical models to capture complex relationships

Associations of F&V Consumption with Smoking and Alcohol Intake
NIH-AARP Diet and Health Study

<table>
<thead>
<tr>
<th>Intake</th>
<th>Current Smokers</th>
<th>Alcohol ≥15 g/d</th>
<th>Alcohol ≥15 g/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st Quartile</td>
<td>21.8</td>
<td>38.3</td>
<td>26.6</td>
</tr>
<tr>
<td>5th Quartile</td>
<td>16.9</td>
<td>32.1</td>
<td>20.6</td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st Quartile</td>
<td>16.9</td>
<td>32.1</td>
<td>20.6</td>
</tr>
<tr>
<td>5th Quartile</td>
<td>6.2</td>
<td>22.7</td>
<td>10.3</td>
</tr>
</tbody>
</table>

George et al. Am J Clin Nutr 2009

Cohort XO
- F&V: NHANES 2003-2006
- n=20,470

Prospective cohort
- n=463,338
- 50-71 y

Quantity vs. Variety of F&V Intake on Cancer Risk
Zutphen Elderly Study

<table>
<thead>
<tr>
<th>Intake (g/d)</th>
<th>Variety (tertile)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Vegetables</td>
<td>1.0</td>
</tr>
<tr>
<td>Fruit</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Jansen et al. Nutr Cancer 2004

Trichopoulou et al. BMJ 2009
What is the Question?
Usual Categories for Statistical Adjustment

- Age
- Sex
- Physical activity
- Body Mass Index
- Smoking/tobacco
- Education/SES
- Hormone status (F)
- Reproductive status (F)

What is the Question?
Usual Categories for Statistical Adjustment

- Age
- Sex
- Physical activity
- Body Mass Index
- Smoking/tobacco
- Education/SES
- Hormone status (F)
- Reproductive status (F)
- Alcohol
- Red meat
- Processed meat
- Fish
- Cereal fiber
- Dietary supplements
- Fruit (for vegetables)
- Vegetables (for fruit)

What is Not a Fruit or Vegetable?

- Fruit: dried, juice?
- Vegetable: potatoes/other tubers, legumes, juice?

Fruit and Vegetable Intake and Overall Cancer Risk
European Prospective Investigation into Cancer and Nutrition

<table>
<thead>
<tr>
<th>Q (g/d)</th>
<th>Cases</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-226</td>
<td>6163</td>
<td>1.00</td>
<td>~</td>
</tr>
<tr>
<td>227-338</td>
<td>6194</td>
<td>0.95</td>
<td>0.92-0.99</td>
</tr>
<tr>
<td>339-462</td>
<td>6263</td>
<td>0.91</td>
<td>0.88-0.95</td>
</tr>
<tr>
<td>463-646</td>
<td>6482</td>
<td>0.93</td>
<td>0.89-0.97</td>
</tr>
<tr>
<td>≥647</td>
<td>5502</td>
<td>0.89</td>
<td>0.85-0.93</td>
</tr>
</tbody>
</table>

Prospective cohort
- n=478,478
- 25-70 y
- 8 y f/u

Under the assumption that study subjects shift one quintile upward in the distribution of F&V intake corresponding to an average increase of ~150 g/d, 2.6% cancers in men and 2.3% cancers in women could be avoided.

Given the small magnitude of the observed associations, caution should be applied in their interpretation.
Colorectal Cancer Risk in “Dietary Approaches to Stop Hypertension” Pattern

**Prospective cohort**
- n=132,746
- 30-55 y
- ≤26 y f/u

<table>
<thead>
<tr>
<th></th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>1.00</td>
<td>0.83</td>
<td>0.86</td>
<td>0.79</td>
<td>0.81</td>
</tr>
<tr>
<td>Women</td>
<td>1.00</td>
<td>0.81</td>
<td>0.84</td>
<td>0.76</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Fung et al. Am J Clin Nutr 2010

F&V Intake >1500 g/d is Associated with Lower Plasma Biomarkers of Inflammation

Cohort XO
- n=120
- 20.8±2.6 y

- CRP
- Hcys
- IL-6
- TNFα

Descending trend (P<0.05) for ICAM1, TNFα, and NFκB gene expression in PBMC

Hermsdorff et al. Nutr Metabol 2010

Conclusions
- Benefits of F&V when adjusted for other foods and lifestyle factors are modest
- Benefits of F&V are likely mediated both by their constituent nutrients, substitution for energy dense foods, and associated lifestyle factors
- Dietary patterns contribute more importantly to risk of cancer than a specific food group

Accuse not Nature!
She has done her part;
Do Thou but Thine

John Milton, *Paradise Lost* 1667