Does Processing of Foods Impact Cancer Risk?

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Acknowledgements

Sue Monckton –will be missed! - nomination
Marla Todd - nomination
Tanner Selection Committee
Fred Tanner
UIUC faculty member 1923-1956
IFT President 1945-46
Influential in the establishment of the Department of Food Science in Urbana/Champaign in 1948
Reference Article

Can Food Processing Enhance Cancer Protection?
Erdman, Jeffery, Hendrickx, Cross and Lampe.

Nutrition Today (in press, 2014)
Based upon symposium at the 2013 American Institute for Cancer Research Meeting
Outline of Presentation

• Food processing – a perspective
• Cancer incidence – role of diet
• Ying and Yang of processing foods
• Illinois studies on prostate cancer
• Recommendations/ Conclusions
What is Food Processing?

It is the transformation of raw ingredients into food, or of food into other forms

Historical Look

“The growth of towns and cities involved larger needs (for food) and new difficulties in storage and transportation ….. gradually transformed food production from an occupation to a business”

Prescott and Proctor. Food Technology. 1935
Prehistoric Food Processing Procedures

- Fermentation
- Sun Drying
- Preservation with salt
- Various types of heating and smoking
Modern Industrial Food Processing

- Fermentation (with and without salt)
- Dehydration - sun, spray, freeze, hot air, etc.
- Thermal procession – canning (Appert), pasteurization (Pasteur), UHT, etc.
- Separations – dry milling, membrane, centrifugation, etc.
- Freezing – (Birdseye) and refrigeration
Benefits

• Protection from microbiological and chemical hazards
• Provision of a diversity of foods year-round
• Reduction of food shortages
• Reduction of spoilage while maintaining consistent taste and acceptability
• Increase convenience and reduce time needed to prepare foods
Cancer Incidence

• Does it vary throughout the world?

• Genetics and/or Environment?
Age-standardised rates of common cancers

USA

Age-standardised rate per 100 000

Prostate, Lung, Colorectum, Bladder, Melanoma, Breast, Lung, Colorectum, Endometrium, Ovary

Data from International Agency for Research on Cancer\textsuperscript{20}
Age-standardised rates of common cancers in China

Age-standardised rate per 100,000

- Men: Stomach, Lung, Liver, Oesophagus, Colorectum
- Women: Stomach, Lung, Breast, Liver, Oesophagus

Data from International Agency for Research on Cancer

[Graph showing age-standardised rates per 100,000 for common cancers in China, with bars indicating rates for men and women separately.]
Estimated Deaths

**Male**
- Lung & bronchus: 90,810 (31%)
- Prostate: 28,660 (10%)
- Colon & rectum: 24,260 (8%)
- Pancreas: 17,500 (6%)
- Liver & intrahepatic bile duct: 12,570 (4%)

**Female**
- Lung & bronchus: 71,030 (26%)
- Breast: 40,480 (15%)
- Colon & rectum: 25,700 (9%)
- Pancreas: 16,790 (6%)
- Ovary: 15,520 (6%)
Genetics or Environment?

• **Smoking** is a major environmental factor

  – 90% of lung cancer is related to smoking

  – 30% of all cancers are related to smoking
Prostate Cancer International Incidence Rates

- Shanghai, China: 2
- Singapore (Chinese): 10
- Israel: 24
- Saarland, Germany: 36
- Geneva, Switzerland: 49
- USA Seer (White): 101
- USA Seer (Black): 137

Genetics or Environment?

• Both are important!
• Genetics is more related to early onset, aggressive cancers

How much will dietary choices impact cancer incidence, severity and timing?

• Sir Richard Doll predicted in 1981 that 35% of cancer incidence was due to dietary factors
Ying -Yang of Food Processing
Ying - Yang of Cooking

- Excess heat reduces vitamin C, folic acid, and some B vitamins

- Appropriate heating reduced food safety concerns and enhances digestibility of foods and bio-accessibility to nutrients for absorption
Lycopene bioavailability enhanced by:

Cooking releases lycopene by disrupting cell walls and tissue structures.

Heat weakening and dissociates lycopene-protein complexes.

Heat dissolves crystalline lycopene aggregates.

Result is that heat enhances absorption of lycopene.
Blood Lycopene following Daily Intake of Processed Foods

Allen et al., Nutrition & Cancer, 2003
Buccal Mucosal Lycopene Concentrations

Evidence strongly suggests:

• Enhanced colorectal cancer risk with high intake of processed meats
• An association of high intake of salted fish and oral cancer
• Cooking meat to “well-done” (grilling or charbroiling) can produce a variety of carcinogens
• Curing with salt, nitrate or nitrite, or by smoking can increase cancer risk
Cooked and Cured Meat

Meta analysis of studies of red and processed meat and *gastric cancer* risk

1. Processed meat consumption associated with 45% increased risk
2. High intakes of beef, bacon, ham and sausage are risky
3. No association found with pork

Zhu et al, PLOS ONE (Aug, 2013)
What should we do regarding red meat?

- Limit the number of weekly servings processed and smoked meat
- Heat/grill meats at lower temperatures
- Avoid having fat drop directly on coals or a direct flame
- Control portion size
What fermented foods do we eat?

- legumes
- grains
- vegetables
- fruit
- milk
- fish
- meat

**North America**
- Sauerkraut
- Relishes
- Sourdough breads
- Cultured milk
- Mikyuk (Alaska)

**Central & South America**
- Curdito
- Chocolate

**Western Europe & Russia**
- Sauerkraut
- Sourdough breads
- Salami
- Cultured milk

**Africa & Mid-East**
- Grain gruels
- Injera (Ethopia)
- Kumi
- Kefir

**SE Asia**
- Paneer
- Tempeh (Indonesia)
- Idli (India)
- Fish sauces

**Japan, Korea, China**
- Kimchi
- Natto
- Soy sauce
- Fish
- Fish sauces

Pickling
(fermenting in water with or without salt)

- Preserving, soaking or storing in vinegar or brine/salt.
- Fermentation products generated:
  - May cause adverse effects:
    - \( N \)-nitroso compounds (NOCs), mycotoxins
  - May offer health benefits:
    - anti-microbial; viable bacteria in non-pasteurized products

Kimchi
Salted Fish Intake and Oral Cancer

- High rates in Hong Kong, Singapore, southern China.
- 28% increased risk of oral cancer
- Association appears stronger for early life exposure to salted fish (0-3 y)

AICR/WCRF: http://dietandcancerreport.org
Pickled Food and **Gastric Cancer:**
Meta analysis of 60 studies

- high-risk for gastric cancer when pickled foods are eaten daily

### RESULTS

**Overall Risk of Gastric Cancer:**

- OR = 1.52 (95% CI 1.37–1.68)

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<table>
<thead>
<tr>
<th>No.</th>
<th>Study</th>
<th>Exposure</th>
<th>Cancer cases (exposed)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acheson, 1964 (Oth)</td>
<td>Pic. food</td>
<td>69/31</td>
<td>0.70 (0.49–1.01)</td>
</tr>
<tr>
<td>2</td>
<td>Crane, 1970 (Kor)</td>
<td>Pic. veg</td>
<td>167/9</td>
<td>1.06 (0.61–1.85)</td>
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<td>3</td>
<td>Han, 1972 (Oth)</td>
<td>Pic. veg</td>
<td>4/171</td>
<td>1.09 (0.61–1.95)</td>
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<tr>
<td>4</td>
<td>Hoenigsel, 1976 (Jap)</td>
<td>Veg. veg</td>
<td>4/171</td>
<td>1.30 (0.83–2.04)</td>
</tr>
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<td>5</td>
<td>Kono, 1988 (Jap)</td>
<td>Veg. veg</td>
<td>178/102</td>
<td>1.02 (0.73–1.44)</td>
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<td>6</td>
<td>You, 1988 (Kor)</td>
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<td>536/30</td>
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<td>7</td>
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<td>8</td>
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<td>208/21</td>
<td>0.84 (0.63–1.11)</td>
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<td>9</td>
<td>Hirose, 1992 (Jap)</td>
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<td>7/105</td>
<td>0.65 (0.48–0.89)</td>
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<td>1089/108</td>
<td>1.52 (1.24–1.86)</td>
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<td>11</td>
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<td>186/27</td>
<td>3.38 (2.79–4.99)</td>
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<td>12</td>
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<td>62/47</td>
<td>1.60 (0.95–2.68)</td>
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<td>1.41 (0.93–2.13)</td>
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<td>Chen, 1999 (Kor)</td>
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<td>42/58</td>
<td>1.38 (0.71–2.71)</td>
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<td>1.34 (0.85–2.16)</td>
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<td>Huang, 2000 (Kor)</td>
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<td>115/50</td>
<td>1.15 (0.82–1.61)</td>
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<td>18</td>
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<td>96/81</td>
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<td>21</td>
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<td>274/36</td>
<td>1.36 (0.91–2.02)</td>
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<td>22</td>
<td>Kanbara, 2002 (Oth)</td>
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<td>56/40</td>
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<td>Kim, 2002 (Kor)</td>
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<td>24</td>
<td>Sriampond, 2003 (Kor)</td>
<td>Veg. veg</td>
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<td>2.90 (2.03–3.90)</td>
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<td>25</td>
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<td>83/56</td>
<td>2.53 (1.52–4.11)</td>
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<td>26</td>
<td>Bao, 2003 (Kor)</td>
<td>Veg. veg</td>
<td>133/115</td>
<td>1.13 (1.33–1.56)</td>
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<td>27</td>
<td>Cai, 2003 (Kor)</td>
<td>Veg. veg</td>
<td>251/130</td>
<td>1.35 (1.05–1.73)</td>
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<td>28</td>
<td>Chen, 2003 (Kor)</td>
<td>Veg. veg</td>
<td>263/138</td>
<td>1.74 (1.34–2.28)</td>
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<td>29</td>
<td>Fei, 2003 (Kor)</td>
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<td>2.97 (2.34–3.93)</td>
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<td>30</td>
<td>Ito, 2003 (Kor)</td>
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<td>50/19</td>
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<td>31</td>
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<td>Veg. veg</td>
<td>32/23</td>
<td>1.35 (1.04–1.78)</td>
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<td>32</td>
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<td>Veg. veg</td>
<td>81/83</td>
<td>1.96 (1.29–2.99)</td>
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<td>33</td>
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<td>Veg. veg</td>
<td>13/12</td>
<td>2.94 (1.02–8.08)</td>
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<td>34</td>
<td>Li, 2004 (Kor)</td>
<td>Veg. veg</td>
<td>45/27</td>
<td>1.74 (1.32–2.28)</td>
</tr>
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<td>35</td>
<td>Lisowski, 2004 (Kor)</td>
<td>Veg. veg</td>
<td>114/84</td>
<td>1.14 (0.89–1.47)</td>
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<td>36</td>
<td>Machida-Montani, 2004 (Kor)</td>
<td>Veg. veg</td>
<td>70/52</td>
<td>0.63 (0.36–1.13)</td>
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<tr>
<td>37</td>
<td>Li, 2005 (Kor)</td>
<td>Veg. veg</td>
<td>19/6</td>
<td>0.28 (0.08–1.02)</td>
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<td>38</td>
<td>Nan, 2005 (Kor)</td>
<td>Veg. veg</td>
<td>255/166</td>
<td>1.57 (1.22–2.01)</td>
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<td>39</td>
<td>Shintumakane, 2006 (Kor)</td>
<td>Veg. veg</td>
<td>54/21</td>
<td>0.95 (0.71–1.27)</td>
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<tr>
<td>40</td>
<td>Xiao, 2007 (Kor)</td>
<td>Veg. veg</td>
<td>48/49</td>
<td>1.96 (1.08–3.56)</td>
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<tr>
<td>41</td>
<td>Xu, 2008 (Kor)</td>
<td>Veg. veg</td>
<td>144/58</td>
<td>2.00 (1.15–3.49)</td>
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<tr>
<td>42</td>
<td>Chi, 2009 (Kor)</td>
<td>Veg. veg</td>
<td>107/107</td>
<td>1.67 (1.01–2.74)</td>
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<tr>
<td>43</td>
<td>Li, 2009 (Kor)</td>
<td>Veg. veg</td>
<td>196/82</td>
<td>1.96 (1.32–2.90)</td>
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<td>Shen, 2009 (Kor)</td>
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<td>116/182</td>
<td>1.46 (1.17–1.82)</td>
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<td>60/33</td>
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<td>46</td>
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<td>42/58</td>
<td>2.58 (1.40–4.75)</td>
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<td>47</td>
<td>Zhang, 2009 (Kor)</td>
<td>Veg. veg</td>
<td>327/43</td>
<td>2.44 (1.37–4.37)</td>
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<td>48</td>
<td>Lazarivc, 2010 (Kor)</td>
<td>Veg. veg</td>
<td>32/30</td>
<td>2.02 (1.21–3.30)</td>
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<td>49</td>
<td>Zhao, 2011 (Kor)</td>
<td>Veg. veg</td>
<td>32/30</td>
<td>3.00 (1.64–5.69)</td>
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<tr>
<td>50</td>
<td>Zhao, 2011 (Kor)</td>
<td>Veg. veg</td>
<td>1/1</td>
<td>1.00 (0.00–1.00)</td>
</tr>
</tbody>
</table>

**NOTE:** Weighted mean from random effects analysis
Meta analysis of studies of vegetables and gastric cancer risk:

- Fresh vegetables
  OR = 0.62, 95% CI = 0.46–0.85

- Pickled vegetables
  OR = 1.28, 95% CI = 1.06–1.53

Fermented Foods and Cancer
What do we do?

- Generally in the U.S. there is limited intake of pickled/fermented foods and salted foods - Moderation

- They are usually not consumed in isolation

- Fermented dairy products generally provide health benefits, especially if there are live cultures

- Future observational studies will benefit from distinguishing more explicitly between different types of fermented foods
Crucifers lower risk for cancers more effectively than do vegetables, in general

<table>
<thead>
<tr>
<th></th>
<th>RR</th>
<th>Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td>All vegetables</td>
<td>0.75 (p=0.43)</td>
<td>Voorrips et al, 2000</td>
</tr>
<tr>
<td>Cruciferous</td>
<td>0.51 (p=0.004)</td>
<td>(low verses high quintile)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>RR</th>
<th>Prostate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All vegetables</td>
<td>0.81 (p=0.15)</td>
<td>Cohen et al, 2000</td>
</tr>
<tr>
<td>Cruciferous</td>
<td>0.54 (p=0.01)</td>
<td>(ratio &lt;1:&gt;3 servings/wk)</td>
</tr>
</tbody>
</table>
Broccoli retains substantial amounts of vitamin C during home processing, depending upon the cooking method.

<table>
<thead>
<tr>
<th>Cooking Method</th>
<th>Vitamin C (mg/100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw Broccoli</td>
<td>117</td>
</tr>
<tr>
<td>High pressure</td>
<td>88</td>
</tr>
<tr>
<td>Steam</td>
<td>117</td>
</tr>
<tr>
<td>Microwave</td>
<td>64</td>
</tr>
<tr>
<td>Boiling</td>
<td>86</td>
</tr>
</tbody>
</table>

150 g fresh-cut Marathon broccoli

Vallejo et al, 2002
**BUT** glucosinolates require hydrolysis to produce the anti-carcinogen - sulforaphane.

Glucoraphanin $\xrightarrow{\text{Myrosinase}}$ ITC

Sulforaphane $\xrightarrow{}$ Glucoraphanin

I sothiocyanate Anticarcinogen
Impact of thermal processing on sulforaphane formation in broccoli.
Marathon broccoli (n=3; 100 g each, a compilation from 4 heads) was heated by a) microwave in a covered dish with 30 mL water; b) boiling in 1L water; c) steaming.
Comparison of Heating Methods for Optimizing GP Hydrolysis to Sulforaphane

- Microwave Heating
- Boiling
- Steaming

Graph showing the comparison of Sulforaphane (µmol/g ww) levels over time (min) for different heating methods.
Fact 1: the health effects of broccoli are strong and deserve to be harnessed.

Fact 2: sulforaphane is so unstable, the plant keeps it conjugated (as glucoraphanin) - when free it rapidly degrades.

Fact 3: this stable conjugate requires an enzyme myrosinase to release sulforaphane.

Fact 4: Broccoli processing should protect myrosinase to provide more dietary sulforaphane.
## Relative Risk of Prostate Cancer

<table>
<thead>
<tr>
<th>Number of Servings</th>
<th>0</th>
<th>1-3/mo</th>
<th>1/wk</th>
<th>2-4/wk</th>
<th>( P ) for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrots</td>
<td>1.0</td>
<td>1.18</td>
<td>1.22</td>
<td>1.14</td>
<td>0.540</td>
</tr>
<tr>
<td>Spinach</td>
<td>1.0</td>
<td>1.00</td>
<td>0.97</td>
<td>1.22</td>
<td>0.510</td>
</tr>
<tr>
<td>Broccoli</td>
<td>1.0</td>
<td>0.96</td>
<td>0.76</td>
<td>1.05</td>
<td>0.170</td>
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<tr>
<td>Tomato Sauce</td>
<td>1.0</td>
<td>0.85</td>
<td>0.77</td>
<td>0.66</td>
<td>0.001</td>
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<tr>
<td>Tomatoes</td>
<td>1.0</td>
<td>0.90</td>
<td>0.91</td>
<td>0.91</td>
<td>0.030</td>
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<tr>
<td>Pizza</td>
<td>1.0</td>
<td>0.94</td>
<td>0.76</td>
<td>0.85</td>
<td>0.050</td>
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<tr>
<td>Tomato Juice</td>
<td>1.0</td>
<td>1.02</td>
<td>0.85</td>
<td>1.15</td>
<td>0.670</td>
</tr>
</tbody>
</table>

Giovannucci et al. *J Natl Cancer Inst* 1995; 87: 1767-76
Lycopene consumption and prostate cancer risk
Health Professional Follow-Up Study

• Zu, K., et al., JNCI 106: online (2014)
  – The Giovannucci group at Harvard confirmed ~6,400 prostate cancer from ~49,000 men enrolled in 1986

– 1986-2010 – lycopene intake and cancer:
  • Total Prostate Cancer (RR: 0.92, \( P = 0.009 \))
  • Lethal Prostate Cancer (RR: 0.72, \( P = 0.04 \))

– One Prior Negative PSA test
  • Total Prostate Cancer (RR: 0.88, \( P = 0.02 \))
  • Lethal Prostate Cancer (RR: 0.47, \( P = 0.009 \))
Impact of Tomato Powder and Lycopene on Chemically-induced Prostate Cancer

• NMU Study in F344 rats on tomato versus lycopene alone

• Design - Diets
  • 10% tomato powder diet
  • Lycopene supplement diet
  • Control AIN-93 diet
  – Fed for over 1 year

Survival By Tomato Treatment

![Graph showing survival by tomato treatment over weeks post-NMU. The graph compares Placebo Beadlets, Lycopene Beadlets, and Tomato Powder. The y-axis represents the percentage of survival, and the x-axis represents weeks post-NMU.]
Impact of Tomato and Broccoli Powder and Lycopene on Transplantable Prostate Tumors

- Transplantable tumor model of prostate cancer in Copenhagen rats
- Tested impact of feeding various dietary treatments including freeze-dried whole tomato powder, broccoli powder or lycopene supplements

Dunning Tumor Weights

P values indicate statistical difference from the control tumor weights.
Broccoli & Tomatoes: Eat Them Together, Life Will Be Better
Impact of Tomato Powder +/- Soy Germ on Prostate Cancer in TRAMP Mice

Zuniga, Erdman and Clinton
University of Illinois
The Ohio State University

Study Design

- 3 wk old male C57BL/6 x FVB TRAMP mice acclimated to modified AIN-93G diet for 1 wk

- Mice randomized to consume experimental diets for 14 weeks

Dietary Treatments

- AIN-93 G Control (n=29)
- 10% Tomato Powder (n=31)
- 2% Soy Germ (n=32)
- 10% Tomato Powder + 2% Soy Germ (n=27)
What is Soy Germ?

- Phytochemical rich fraction of the soybean.
- Potential anti-carcinogenic properties of becoming studied.
- Unique isoflavone profile

Consumption of tomato powder, soy germ, and the combination significantly reduced prostate cancer incidence.
Cooked or Raw?

• Mild cooking enhances the absorption of bioactives from both tomato and broccoli

How Many Servings?

• About 3 servings per week of each vegetable appears to be related to less prostate cancer risk
Conclusions

Peto was correct in 1981—about 35% of cancer related to diet—much has to do with obesity and alcohol—but food and processing choices matter

• Don’t overcook,
• Limit processed red meat consumption
• Maintain weight and exercise
• 2/3 of plate should be plant based

Never too early or too late to follow appropriate general guidelines for cancer reduction

WCRF/AICR web site
www.dietandhealthreport.org
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<th>RECOMMENDATIONS</th>
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<td><strong>BODY FATNESS</strong></td>
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<td>Be as lean as possible within the normal range of body weight</td>
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<td><strong>PHYSICAL ACTIVITY</strong></td>
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<td>Be physically active as part of everyday life</td>
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<td><strong>FOODS AND DRINKS THAT PROMOTE WEIGHT GAIN</strong></td>
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<td>Limit consumption of energy-dense foods</td>
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<td>Avoid sugary drinks</td>
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<td><strong>PLANT FOODS</strong></td>
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<td>Eat mostly foods of plant origin</td>
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<td><strong>ANIMAL FOODS</strong></td>
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<td>Limit intake of red meat and avoid processed meat</td>
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Prostate Gland

http://www.london-urology.co.uk/prostate%20side%20on.jpg