GI/GL and Risk of Diabetes and Cardiovascular Disease: an Epidemiological Perspective

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## Food predictors of type 2 diabetes

<table>
<thead>
<tr>
<th></th>
<th><strong>Nurses’ Health Study</strong></th>
<th><strong>Health Professionals Follow-up Study</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fried potatoes</td>
<td>(+)</td>
<td>Fried potatoes (+)</td>
</tr>
<tr>
<td>Cooked potatoes</td>
<td>(+)</td>
<td>White bread (+)</td>
</tr>
<tr>
<td>Cola beverages</td>
<td>(+)</td>
<td>White rice (+)</td>
</tr>
<tr>
<td>White bread</td>
<td>(+)</td>
<td>Carbonated bevs (+)</td>
</tr>
<tr>
<td>White rice</td>
<td>(+)</td>
<td></td>
</tr>
<tr>
<td>Cold brkfst cereal</td>
<td>(-)</td>
<td>Cold brkfst cereal (-)</td>
</tr>
<tr>
<td>Yogurt</td>
<td>(-)</td>
<td>Yogurt (-)</td>
</tr>
</tbody>
</table>

1. Fried potatoes
2. Cooked potatoes
3. Cola beverages
4. White bread
5. White rice
6. Cold breakfast cereal
7. Yogurt
Slowly Digested Carbohydrate

Blood Glucose

Insulin

Easily Digested Carbohydrate

Blood Glucose

Insulin

Willett, EDBH, 2001
Correlation between baseline insulin resistance and increase in postprandial glucose, insulin, and triacylglycerol after increasing dietary carbohydrate from 40-60% of energy

(n = 10 postmenopausal women)

<table>
<thead>
<tr>
<th>Variables</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>0.68</td>
<td>0.06</td>
</tr>
<tr>
<td>Insulin</td>
<td>0.82</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>Plasma triacylglycerol</td>
<td>0.77</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

(Jeppesen et al. 1997)
Glycemic Load = Glycemic Index x CHO
Fasting Plasma TG Levels by Dietary Glycemic Load Postmenopausal Women with Different BMIs

Liu et al, 2000
Potential Adverse Health Effects of High GI/GL Diets

- Type 2 diabetes
- Coronary heart disease
- Weight gain/adiposity
- Macular degeneration
- Cataract
- Cancer (colon, breast, etc.)
- Gall stones
Relative Risk of Type 2 Diabetes by Different Levels of Cereal Fiber and Glycemic Load

WOMEN

Relative Risk

Cereal Fiber

- High >5.8 g/day
- Medium 2.5 -5.8 g/day
- Low <2.5 g/day

Glycemic Load

- High >165
- Medium 165-143
- Low <143

(Salmeron et al, 1997)
Relative Risk of Type 2 Diabetes by Different Levels of Cereal Fiber and Glycemic Load

(Salmeron et al, 1997)
Results

Joint effects of glycemic index and cereal fiber in the Nurses’ Health Study II

(RRs multivariate and diet adjusted)
Multivariate RRs for association between GI and type 2 diabetes risk

**Study**

- Salmeron et al (6) 1997
- Salmeron et al (7) 1997
- Zhang et al (10) 2006
- Schulze et al (9) 2004
- Fixed overall
- Random overall

**Rate ratio and 95% CI**

- (Barclay AW et al. AJCN, 2008)
A role for the glycemic index in preventing or treating diabetes?¹,²

John M Miles

“Although this study [Sahyoun et al. 2008] had a somewhat shorter duration and smaller sample size than several earlier studies that found an association between GI and diabetes risk, it strengthens the argument that high-GI diets per se do not increase the risk of diabetes.”

Miles J, AJCN, 2008
Pooled relative risk (95% CI) of type 2 diabetes comparing high vs low glycemic index
Dietary glycemic index, glycemic load, and digestible carbohydrate intake are not associated with risk of type 2 diabetes in eight European countries.

Sluijs I, 2013

--Case-cohort study nested within EPIC
--Single baseline assessment of diet
--N = 12,403 cases of type 2 diabetes
--Hi vs Lo Quartile: for GI, RR = 1.05 (95% CI = 0.96, 1.16)
for GL, RR = 1.07 (95% CI = 0.95, 1.20)
--“discrepancies in the GI value assignment to foods possibly explain differences in GI associations with diabetes within the same study population”
Effect of acarbose and placebo on cumulative probability of remaining free of diabetes over time

(Chiasson JL et al. The Lancet, 2002)
Representative abnormal islet from a high-GI animal compared with a normal islet from a weight-matched low-GI animal

Effect of Low GI Diet or HbA1c in Diabetes

### Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean Difference IV,Fixed,95% CI</th>
<th>Weight</th>
<th>Mean Difference IV,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand 1991</td>
<td></td>
<td>8.9 %</td>
<td>-0.90 [-1.92, 0.12]</td>
</tr>
<tr>
<td>Giacco 2000</td>
<td></td>
<td>23.7 %</td>
<td>-0.30 [-0.93, 0.33]</td>
</tr>
<tr>
<td>Gilbertson 2001</td>
<td></td>
<td>34.0 %</td>
<td>-0.60 [-1.12, -0.08]</td>
</tr>
<tr>
<td>Jimenez-Cruz 2003</td>
<td></td>
<td>20.9 %</td>
<td>-0.50 [-1.17, 0.17]</td>
</tr>
<tr>
<td>Komind 2001</td>
<td></td>
<td>3.7 %</td>
<td>-0.18 [-1.76, 1.40]</td>
</tr>
<tr>
<td>Rizkalla 2004</td>
<td></td>
<td>8.8 %</td>
<td>-0.40 [-1.43, 0.63]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td>100.0 %</td>
<td>-0.50 [-0.81, -0.20]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi²=1.31, df=5 (P=0.93); I²=0.0%

P=0.001

Favors low glycemic  Favors control

(Elliott TD 2009, Cochrane Collaboration)
Sugar-sweetened beverage consumption and risk of T2DM, comparing extreme categories of intake (random-effects estimate)

- Montonen, 2007
- Paynter Men, 2006
- Paynter Women, 2006
- Schulze, 2004
- Palmer, 2008
- Bazzano, 2008
- Odegaard, 2010
- Nettleton, 2009
- de Koning, 2010

Combined

1.26 (1.12, 1.41)

Fixed-effects estimate: RR 1.25 (1.17, 1.32)

Omitting 3 studies that adjusted for BMI and total energy:
Random effects: RR 1.28 (1.13, 1.45)
Fixed effects: 1.25 (1.18, 1.34)

(Malik et al. Diabetes Care 2010)
Glycemic index and cardiovascular disease

Ref 1
NHS, n=75521
Incident coronary heart disease
Prospective study
5th vs. 1st quintile

Ref 16
Dutch Women, n=15,714
Incident coronary heart disease and
cerebrovascular accident
Prospective study
4th vs. 1st quartile

Ref 54
Dutch population in Zutphen, n=646
Incident coronary heart disease
Prospective study
3rd vs. 1st tertile

RR or OR (95% CI)
9.200 (Chiu et al.)
NHS
n=75,521
Dutch Women
n=15,714
Dutch Men (Zutphen)
n=646

1.68 1.31 1.02
1.67 1.33 1.07
1.87 1.11 0.66
Figure 2. Effect of Acarbose on the Probability of Remaining Free of Cardiovascular Disease

P = .04 (Log-Rank Test)
P = .03 (Cox Proportional Model)

No. at Risk
Placebo 686 675 667 658 643 638 633 627 615 611 604 519 424 332 232
Acarbose 682 659 635 622 608 601 596 590 577 567 558 473 376 286 203

(Chiasson et al. JAMA, 2003)
What about Potatoes?

- 84,555 women in the Nurses’ Health Study followed for 20 yrs
- 4,496 incident cases of type 2 diabetes
- Highest vs lowest quintile intake of potatoes:
  - MV RR = 1.14 (95% CI: 1.02, 1.26; \( P,\text{trend} = 0.009 \))
- 1 serving potatoes/d vs 1 serving whole grains/d:
  - MV RR = 1.30 (95% CI: 1.08, 1.57)
Relative Risk of Coronary Heart Disease

<table>
<thead>
<tr>
<th>Body Mass Index (kg/M²)</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;23</td>
<td>0.94</td>
</tr>
<tr>
<td>23-29</td>
<td>1.16</td>
</tr>
<tr>
<td>&gt;29</td>
<td>1.19</td>
</tr>
</tbody>
</table>

- Tertile 1 (lowest)
- Tertile 2
- Tertile 3 (highest)

Liu et al., 2000
Pooled Risk Estimate for CHD comparing highest to lowest GI quantiles

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Weight</th>
<th>Relative Risk</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.1 Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liu et al [28]</td>
<td>10.5%</td>
<td>1.31</td>
<td>[1.02, 1.68]</td>
</tr>
<tr>
<td>Beulens et al [31]</td>
<td>9.6%</td>
<td>1.44</td>
<td>[1.10, 1.89]</td>
</tr>
<tr>
<td>Sieri et al Women [33]</td>
<td>4.9%</td>
<td>1.42</td>
<td>[0.90, 2.25]</td>
</tr>
<tr>
<td>Burger et al Women [36]</td>
<td>6.3%</td>
<td>1.18</td>
<td>[0.80, 1.74]</td>
</tr>
<tr>
<td>Levitan et al [42]</td>
<td>13.1%</td>
<td>1.12</td>
<td>[0.92, 1.36]</td>
</tr>
<tr>
<td>Grau et al Women [43]</td>
<td>5.0%</td>
<td>1.38</td>
<td>[0.88, 2.17]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>49.3%</td>
<td>1.26</td>
<td>[1.12, 1.41]</td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 3.01, df = 5 (P = 0.70); I² = 0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 3.84 (P = 0.0001)</td>
<td></td>
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</table>

2.1.2 Men

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Weight</th>
<th>Relative Risk</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Dam et al [29]</td>
<td>4.0%</td>
<td>1.11</td>
<td>[0.66, 1.87]</td>
</tr>
<tr>
<td>Lovitan et al [30]</td>
<td>14.4%</td>
<td>0.99</td>
<td>[0.84, 1.17]</td>
</tr>
<tr>
<td>Sieri et al Men [33]</td>
<td>8.0%</td>
<td>0.96</td>
<td>[0.70, 1.32]</td>
</tr>
<tr>
<td>Mursu et al [35]</td>
<td>8.5%</td>
<td>1.25</td>
<td>[0.92, 1.69]</td>
</tr>
<tr>
<td>Burger et al Men [36]</td>
<td>9.2%</td>
<td>0.84</td>
<td>[0.63, 1.11]</td>
</tr>
<tr>
<td>Grau et al Men [43]</td>
<td>6.7%</td>
<td>0.71</td>
<td>[0.49, 1.02]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>50.7%</td>
<td>0.96</td>
<td>[0.84, 1.11]</td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.01; Chi² = 6.76, df = 5 (P = 0.24); I² = 26%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.54 (P = 0.59)</td>
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</table>

**Total (95% CI)**

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<tr>
<th>Weight</th>
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<tbody>
<tr>
<td>100.0%</td>
<td>1.11</td>
<td>[0.99, 1.24]</td>
</tr>
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</table>

Heterogeneity: Tau² = 0.02; Chi² = 19.89, df = 11 (P = 0.05); I² = 45%
Test for overall effect: Z = 1.71 (P = 0.09)
Test for subgroup differences: Chi² = 8.29, df = 1 (P = 0.004) | I² = 87.9%

(Mirrahimi A et al, JAHA 2012)
What is the best way to characterize carbohydrate quality?

- Industry can game GI by loading foods with fructose
- GI effects depend on amount of carbohydrate $\rightarrow$ GL
- Alternative ways to guide consumers:
  - Whole vs refined grains
  - Carbohydrate : fiber ratio
  - Milled refined grains $\rightarrow$ milled whole grains $\rightarrow$ intact whole grains
Conclusions

1. Dietary glycemic index and load have been hypothesized to increase risk of many conditions; the evidence for type 2 diabetes is now strong.

2. Dietary glycemic index/load and coronary heart disease and cereal fiber have independent relationships with risk of diabetes and cardiovascular disease.

3. The concept of glycemic index is valuable in understanding the effects of diet on risk of chronic disease. Whether this should be part of widespread dietary advice is less clear, but some information on carbohydrate quality is essential.

4. Sugar-sweetened beverages are particularly harmful and a top public health target.