GI – What special people benefit?

David J.A. Jenkins

Department of Nutritional Sciences, Faculty of Medicine,
University of Toronto, Ontario,
Canada

Clinical Nutrition & Risk Factor Modification Center
St. Michael’s Hospital;
Conflict of Interest

- **Griffin Hospital**, New Haven - For the development of the Nuval System. C, H, SAB
- **The Canola & Flax Councils of Canada**. C, H, SAB
- **Pulse Canada** - SAB
- **Saskatchewan Pulse Growers** – SAB
- **Canadian Institute of Health Research (CIHR)** – G
- **Canadian Foundation for Innovation (CFI)** – G
- **Ontario Research Fund (ORF)** – G
- **Advanced Foods and material Network (AFMNet)** – G
- **International Tree Nut Council Nutrition Research and Education Foundation and the Peanut Institute** – G, H
- **Alpro Soy Foundation** - H

C = Consultancies; H = Honorarium; SAB = Scientific Advisory Boards; G = Grants
Conflict of Interest

- **Oldways Preservation Trust**, Boston, MA – A not for profit organization promoting traditionally “healthy” ways of eating (eg. Mediterranean Diet, etc.) H
- **Almond Board of California, Modesto**, CA – A branch of the USDA (therefore “not for Profit”) to promote the use of almonds. C,H,G
- **The California Strawberry Commission**, Watsonville, CA – Another USDA not for profit group to explore possible health benefits and to promote the use of strawberries. SAB
- **Bayer Consumer Care**, Springfield NJ – Marketing of nutritional supplements/nutraceuticals. SAB
- **Orafi**, Tienen, Belgium Development of prebiotics for modification of colonic microflora. SAB, G

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Conflict of Interest

- **Sanitarium Company**, Sydney, Australia – Australia’s largest health food manufacturing company and soy food producer. G, SAB
- **Solae**, St. Louis – The major US producer of soy protein isolate. C, G
- **Barilla**, Italy – A general food company. Producer of pasta and baked goods. G
- **Haine Celestial**, CA – One of the largest Health Food companies in the US. G
- **Loblaws Supermarkets** – Canada’s largest supermarket chain. G, SAB
- **Unilever**, Vlaardingen, Netherlands – Major margarine producers including Becel and Take Control (plant sterol enriched margarine). G, GP

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Conflict of Interest

- **Herbalife International**, Century City, CA – A nutraceutical company with an emphasis on sourcing plant derived components for weight loss.  SAB

- **Nutritional Fundamentals for Health**, Montreal, QE – A new nutraceutical company exploring and aiming to market food derived components for health. SAB

- **Pacific Health Laboratories INC**, Matawan, NJ – a nutrition technology company with functional food and nutraceutical products researched and commercialized for sports performance weight loss and type 2 diabetics which can be marketed without prior approval of the FDA. SAB, Stock

- **Metagenics/MetaProteomics**, Gig Harbor WA – a company assessing natural products from hops which will positively impact individuals with specific genetic susceptibilities for chronic disease. SAB

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Conflict of Interest

- **Agriculture and Agrifoods Canada (AAFC)** – SAB
- **Canadian Agriculture Policy Institute (CAPI)** – SAB
- **White wave-Dean Foods**, Colorado – SAB, C, H
- **The Coco Cola sugar Advisory Board**. C, H, SAB
- **Orafti**, Tienen, Belgium Development of prebiotics for modification of colonic microflora. SAB, G
- **Wife and is a Director of Glycemic Index Laboratories**, Toronto, CA – Financial relationship of a spouse
- **Kellogg’s**, Canada – C, H, SAB
- **Quaker Oats**, Canada-C, H, SAB

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Common ways of Reducing post prandial glycemia

1) Improving blood glucose disposal
   direct tissue sensitization: biguanides (metformin), thiazolidinediones; or increase insulin: sulfonylureas, DPP4 inhibitors, incretins/analogues; insulin itself

2) Increasing glucose losses
   SGLT2 inhibitors – urine; Bypass surgery- Small intestine

3) Reducing the amount of “bad” carbohydrates
   by increasing fat calories, ↑ fat, ↑ protein (Atkins) low GI/GL diets, olive oil, nuts(PREDIMED)

4) Altering the Quality carbohydrate to a “lente” (slow release) form
   Acarbose, Low GI/GL diets, ↑ fat, ↑ protein, gastric banding

To Discuss # 3 & 4
3) Reducing the amount of dietary carbohydrate 

by increasing fat calories, ↑ fat, ↑ protein (Atkins), olive oil, nuts (PREDIMED), low GI/GL diets
Reducing Glycemic Load
Reducing Carbohydrate (-3%) with Fat (+4%)

PREDIMED Study

Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)

Control

Nuts {30%}

Olive Oil {30%}

↓ GL ↓ GI ?

Med diet, EVOO: hazard ratio, 0.70 (95% CI, 0.53–0.91); P=0.009
Med diet, nuts: hazard ratio, 0.70 (95% CI, 0.53–0.94); P=0.02

Reducing Glycemic Load

CHD: Dietary Patterns: Vegetable Oil and Vegetable Protein

Nurses’ Health Study: Low-CHO-Diet Score and Risk of CHD

Intake of Carbohydrate, Animal Protein and Animal Fat

Intake of Carbohydrate, Vegetable Protein and Vegetable Fat

Reducing Glycemic Load
Diabetes: Dietary Patterns: Vegetable Oil and Vegetable Protein
Nurses’ Health Study: Low-CHO-Diet Score and Risk of Diabetes

Swapping CH$_2$O for SFA
Increasing Glycemic Load
DANISH PROSPECTIVE COHORT: Diet, Cancer and Health
n=53,644 men and women

Effect of replacement of 5% energy from SFA with 5% energy from carb

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Replace 5% of energy from SFA with</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low-GI</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0.88 (0.72, 1.07)</td>
</tr>
</tbody>
</table>

Higher/ Medium GI diets = SFA replacement nutrient

4) Altering the Quality carbohydrate as a “lente” (slow release) form

Acarbose, Viscous fibers, Low GI/GL diets, ↑ fat, ↑ protein, gastric banding
We can reduce rate of absorption ("Lente", Carbohydrate) with Acarbose.

Acarbose
Viscous Fibers
Low glycemic foods

FIGURE 1. Hypothetical effect of feeding diets with a low (A) or high (B) glycemic index on gastrointestinal glucose absorption and postprandial blood glucose.
Fig. 2—Mean change in blood glucose in 8 subjects over the 2 h after test meals of control crispbread with placebo tablet, guar crispbread with placebo tablet, control crispbread with acarbose tablet, and guar crispbread with acarbose tablet.

Jenkins DJ et al. Lancet 1979;2(8149):924-7
STOP-NIDDM Trial

CVD Events
Acarbose
↓ 49% RR

STOP-NIDDM Trial

Hypertension (new cases)

Acarbose ↓ 34% RR

Women more than Men?

Glycemic Load & T2DM in Adults


<table>
<thead>
<tr>
<th>First author, year (ref.) and ethnicity</th>
<th>No. subjects (x100)</th>
<th>RR</th>
<th>LCI</th>
<th>UCI</th>
<th>%WT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krishnan 2007 (52)</td>
<td>40,078</td>
<td>1.34</td>
<td>1.00</td>
<td>1.80</td>
<td>4.94</td>
</tr>
<tr>
<td>Meyer 2000 (12)</td>
<td>35,988</td>
<td>0.85</td>
<td>0.53</td>
<td>1.36</td>
<td>3.03</td>
</tr>
<tr>
<td>Hopping 2010 (17) JA</td>
<td>18,672</td>
<td>1.15</td>
<td>0.90</td>
<td>1.48</td>
<td>5.53</td>
</tr>
<tr>
<td>Halton 2008 (16) &amp; Mekary 2011 (30)</td>
<td>83,443</td>
<td>2.13</td>
<td>0.82</td>
<td>5.55</td>
<td>1.02</td>
</tr>
<tr>
<td>Salmerón 1997 (6)</td>
<td>65,173</td>
<td>1.86</td>
<td>1.23</td>
<td>2.82</td>
<td>3.55</td>
</tr>
<tr>
<td>Schulze 2004 (53)</td>
<td>91,249</td>
<td>1.35</td>
<td>0.73</td>
<td>2.49</td>
<td>2.13</td>
</tr>
<tr>
<td>Zhang 2006 (15)</td>
<td>13,110</td>
<td>2.21</td>
<td>1.05</td>
<td>4.65</td>
<td>1.58</td>
</tr>
<tr>
<td>Hopping 2010 (17) NH</td>
<td>5941</td>
<td>1.35</td>
<td>1.06</td>
<td>1.72</td>
<td>5.65</td>
</tr>
<tr>
<td>Villegas 2007 (54)</td>
<td>64,227</td>
<td>1.46</td>
<td>1.22</td>
<td>1.76</td>
<td>6.49</td>
</tr>
<tr>
<td>Hopping 2010 (17) CA</td>
<td>14,643</td>
<td>1.84</td>
<td>1.23</td>
<td>2.75</td>
<td>3.67</td>
</tr>
<tr>
<td><strong>Subtotal</strong> (I² = 29.7%, P = 0.172)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>P &lt; 0.001</td>
<td>1.40</td>
<td>1.23</td>
<td>1.60</td>
</tr>
</tbody>
</table>

| Male                                    |                     |      |      |      |      |
| Hopping 2010 (17) JA                   | 16,572              | 1.05 | 0.87 | 1.28 | 6.36 |
| Hopping 2010 (17) NH                   | 4568                | 1.09 | 0.81 | 1.47 | 4.86 |
| Sakurai 2011 (55)                      | 1995                | 1.15 | 0.66 | 2.02 | 2.40 |
| Hopping 2010 (17) CA                   | 15,116              | 1.58 | 1.17 | 2.12 | 4.87 |
| Simila 2011 (13)                       | 25,943              | 0.73 | 0.42 | 1.25 | 2.52 |
| Salmerón 1997 (5)                      | 42,759              | 1.43 | 0.85 | 2.40 | 2.67 |
| **Subtotal** (I² = 42.1%, P = 0.124)  |                     |      |      |      |      |
|                                        |                     | P = 0.132 | 1.16 | 0.96 | 1.40 |

| Mixed sexes                             |                     |      |      |      |      |
| Stevens 2002 (8) AA                     | 2722                | 0.98 | 0.81 | 1.18 | 6.43 |
| Stevens 2002 (8) EA                     | 9529                | 1.26 | 1.01 | 1.57 | 5.98 |
| Mosdøl 2007 (9)                         | 5598                | 0.70 | 0.27 | 1.84 | 1.01 |
| Hodge 2004 (7)                          | 31,641              | 0.99 | 0.58 | 1.69 | 2.56 |
| Patel 2007 (37)                         | 124,907             | 1.24 | 1.09 | 1.40 | 7.29 |
| Sahyoun 2008 (10)                       | 1898                | 1.28 | 0.48 | 3.36 | 1.00 |
| Sluijs 2010 (14)                        | 37,846              | 3.09 | 1.66 | 5.73 | 2.09 |
| van Woudenbergh 2011 (11)               | 4366                | 1.01 | 0.47 | 2.17 | 1.49 |
| **Subtotal** (I² = 55.3%, P = 0.029)   |                     |      |      |      |      |
|                                        |                     | P = 0.060 | 1.19 | 0.99 | 1.44 | 100.0 |

| Overall (I² = 48.3%, P = 0.005)         |                     |      |      |      |      |
|                                        |                     | P < 0.001 | 1.27 | 1.15 | 1.40 | 100.0 |

Random effects analysis

0.7 1 1.272.0 3.0 4.5
Worse Better
Women more than Men?  
GL & CHD Risk

Pooled Risk Estimate for CHD comparing highest to lowest GL quantiles

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Weight</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>3.1.1 Women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beulens et al [31]</td>
<td>8.2%</td>
<td>1.44 [0.95, 2.19]</td>
</tr>
<tr>
<td>Sieri et al Women [33]</td>
<td>5.3%</td>
<td>2.45 [1.38, 4.36]</td>
</tr>
<tr>
<td>Halton et al [34]</td>
<td>6.5%</td>
<td>1.90 [1.15, 3.14]</td>
</tr>
<tr>
<td>Burger et al Women [36]</td>
<td>6.7%</td>
<td>0.93 [0.57, 1.52]</td>
</tr>
<tr>
<td>Levitan et al [42]</td>
<td>11.4%</td>
<td>1.22 [0.90, 1.65]</td>
</tr>
<tr>
<td>Grau et al Women [43]</td>
<td>8.0%</td>
<td>2.11 [1.37, 3.24]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>46.1%</td>
<td>1.55 [1.18, 2.03]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.06; Chi² = 11.55, df = 5 (P = 0.04); I² = 57%
Test for overall effect: Z = 3.14 (P = 0.002)

3.1.2 Men

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Weight</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>van Dam et al [29]</td>
<td>3.9%</td>
<td>1.05 [0.52, 2.13]</td>
</tr>
<tr>
<td>Levitan et al [30]</td>
<td>13.0%</td>
<td>1.04 [0.80, 1.35]</td>
</tr>
<tr>
<td>Sieri et al Men [33]</td>
<td>8.1%</td>
<td>1.14 [0.75, 1.74]</td>
</tr>
<tr>
<td>Mursu et al [35]</td>
<td>10.2%</td>
<td>1.11 [0.79, 1.56]</td>
</tr>
<tr>
<td>Burger et al Men [36]</td>
<td>9.6%</td>
<td>1.08 [0.75, 1.55]</td>
</tr>
<tr>
<td>Grau et al Men [43]</td>
<td>9.2%</td>
<td>1.11 [0.76, 1.62]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>53.9%</td>
<td>1.08 [0.93, 1.26]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 5 (P = 1.00); I² = 0%
Test for overall effect: Z = 1.05 (P = 0.29)

Total (95% CI) 100.0% 1.27 [1.09, 1.49]

Heterogeneity: Tau² = 0.03; Chi² = 19.33, df = 11 (P = 0.06); I² = 43%
Test for overall effect: Z = 3.06 (P = 0.002)
Test for subgroup differences: Chi² = 5.11, df = 1 (P = 0.02), I² = 80.4%

Mirrahimi A, Jenkins D et. al. JAHA 2012;1:e000752
Who Else Benefits?
Baseline SBP Level determines HbA1c Reduction by Canola oil-Low GL Diet

Changes from Baseline (Week 0) in HbA1c (% HbA1c unit) during Canola oil-Low GL (test) and High Wheat-Fibre (control) Diets in Participants stratified by high and low baseline SBP. HbA1c was reduced more on the test than the control for those with higher baseline SBP (P<0.003).
Baseline Waist: Height Ratio and CVD Risk Level determines HbA1c Reduction by Canola oil-Low GI Diet

Changes from Baseline (Mean of Week -1 and 0) in HbA1c (% HbA1c unit) during Canola oil-Low GL (test) and High Wheat-Fibre (control) Diets in Participants stratified by Baseline Waist: Height Ratio and Baseline CVD risk.
Insulin Response Determines Weight Loss

- Low-Glycemic Load Diet
- Low-Fat Diet

Insulin Concentration ≤ 57.5 μIU/mL at 30 min After 75-g Dose of Oral Glucose

30 min Insulin < 57.5 μIU/mL

Change From Baseline, kg

Time, mo

P = .90

Insulin Concentration > 57.5 μIU/mL at 30 min After 75-g Dose of Oral Glucose

30 min Insulin > 57.5 μIU/mL

Change From Baseline, kg

Time, mo

P = .02

BMI Determines CHD Risk dependent on glycemic load:
10y of follow-up in the Nurses Health Study (n=65,000)

Insulin resistance determines GI effect in producing FATTY LIVER (NAFL) and GI

FIGURE 1. The percentage prevalence of high-grade liver steatosis by group of dietary glycemic index (GI) [low GI: first 3 quartiles (■) compared with high GI: 4th quartile (□)] in insulin-sensitive (first 3 quartiles of homeostasis model assessment–insulin resistance) and insulin-resistant (4th quartile of homeostasis model assessment–insulin resistance) subjects. P values are chi-square statistics. GI subgroup × insulin sensitivity status interaction was significant for liver steatosis grade, P = 0.002.

Glycemic Load and CRP at High and Low BMI

1. Slowing carbohydrate absorption (e.g. low GI diets / Acarbose) is likely to be most effective in those with greatest insulin resistance and CVD risk.

2. Is this conclusion valid for other treatment approaches?