The Effect of Applying the FDA Definition of Whole Grains to Health Claims for Risk Reduction of Cardiovascular Disease and Diabetes

Michael Falk, Ph.D.
Life Sciences Research Office, Inc.

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The Process

- Since 1962 LSRO has provided scientific analysis and advice to government and industry
  - Non-profit, independent, impartial
- In conjunction with an external panel of experts
  - Nutrition, cereal chemistry, epidemiology, FDA regulations
- The project was sponsored by Kellogg, Co.
  - Hands-off, no input into the panel selection, design, or outcome
Goals

- Evaluate the “whole grain” literature to see if it supports selected scientific relationships based on AACC/FDA definition of whole grains (CVD and diabetes)
- Expand the analysis to include other grain components such as bran or fiber and studies that do not explicitly use the term “whole grain”
Health Claims in US

- Risk reduction not curing, treating, mitigating disease
- Based on scientific relationship
- First and foremost based on effects in humans
  - Interventional (RCT)
  - Observational
  - Everything else is considered supplementary
- Require significant scientific agreement or qualifying language (NLEA)
- Based on authoritative statement from an appropriate scientific organization (FDAMA)
Current Health Claims

- Three fiber-related NLEA claims
  - Fruits, vegetables, and grain products that contain fiber, particularly soluble fiber and the risk of CHD (also cancer)
  - Soluble fiber from certain foods and risk of CHD
    - 1st whole-oat sources
    - Then psyllium seed husk
    - Hydrolyzed oat flour
    - Barley and barley products
- Two whole grain FDAMA claims
Current FDAMA Health Claims

- “Diets high in plant foods i.e., fruits, vegetables, legumes and whole grain cereals are associated with lower occurrence of CHD…”

  US National Academy of Sciences
  - Whole grain food must be 51% whole grain ingredients
  - Using FDA definition for whole grain

- Second claim - whole grain food with moderate fat content (refers to the association between low saturated fat and CHD)
AACC/FDA Definition of Whole Grain

“consist of the intact, ground, cracked or flaked caryopsis, whole principal anatomical components – the starchy endosperm, germ and bran – are present in the same relative proportions as they exist in the intact caryopsis”

Literature Search

- Whole Grains and Heart Disease (CVD, heart, CHD, stroke, blood pressure, myocardial infarction..)
- Whole Grains and Diabetes
- 634 potentially relevant articles
- Excluded
  - Reviews, meta-analyses, editorials
  - Animal and *in vitro* studies
- 204 selected for further evaluation
Literature Search (continued)

- **Included (FDA definition)**
  - Human intervention and observational studies
  - Validated endpoints or surrogate endpoint for CVD and/or diabetes
  - Study populations representative of US
  - Healthy populations

- **First analysis - meets FDA definition only**

- **Second analysis expanded definition**
  - Included bran, germ or fiber (the use of products with 25% bran content was commonly included in definition of whole grain in observational studies)
  - Did not explicitly use the term “whole grains” but used whole grains in the study
## Results: CVD Using FDA Definition

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Country</th>
<th>N (Len)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andersson et al. 2007</td>
<td>Randomized Crossover</td>
<td>US</td>
<td>30 (6 wk)</td>
<td>CVD (no significant change)</td>
</tr>
<tr>
<td>Rave et al. 2007</td>
<td>Randomized Crossover</td>
<td>Germany</td>
<td>31 (4 wk)</td>
<td>CVD (no significant change)</td>
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<tr>
<td>Jensen et al. 2004 (HPFS)</td>
<td>Prospective Cohort</td>
<td>US</td>
<td>42,850</td>
<td>CVD (RR=0.82, p=0.01, intake 42.2 vs 3.5 g/d)</td>
</tr>
<tr>
<td>Jensen et al. 2006</td>
<td>Cross-sectional</td>
<td>US</td>
<td>938</td>
<td>CVD (Total cholesterol: -0.16 mmol/L, p=0.02, intake 43.8 vs 8.2 g/d)</td>
</tr>
</tbody>
</table>
## Results: Diabetes Using FDA Definition

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Country</th>
<th>N (Len)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andersson et al. 2007</td>
<td>Randomized Crossover</td>
<td>US</td>
<td>30 (6 wk)</td>
<td>Diabetes (no significant change)</td>
</tr>
<tr>
<td>Rave et al. 2007</td>
<td>Randomized Crossover</td>
<td>Germany</td>
<td>31 (4 wk)</td>
<td>Diabetes (improved insulin and HOMA-IR)</td>
</tr>
<tr>
<td>De Munter et al, 2007 (NHS)</td>
<td>Prospective Cohort</td>
<td>US</td>
<td>73,327</td>
<td>Diabetes (RR=0.63, p&lt;0.001, intake 31.2 vs 3.7 g/d)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>88,410</td>
<td>Diabetes (RR=0.68, p&lt;0.001, intake 39.9 vs 6.2 g/d)</td>
</tr>
</tbody>
</table>
## Results: Expanded Analysis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Design</th>
<th>FDA only</th>
<th>Expanded</th>
<th>Expanded Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD</td>
<td>Intervention</td>
<td>2</td>
<td>15</td>
<td>Beneficial effect</td>
</tr>
<tr>
<td></td>
<td>Observational</td>
<td>2</td>
<td>14</td>
<td>Consistent protective effect</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Intervention</td>
<td>2</td>
<td>10</td>
<td>Suggestive but inconclusive</td>
</tr>
<tr>
<td></td>
<td>Observational</td>
<td>1</td>
<td>11</td>
<td>Suggestive but inconclusive</td>
</tr>
</tbody>
</table>
Report Conclusions

- Using FDA definition as a selection criterion is limiting
  - Historically whole grain definitions have been inconsistent
  - Scientific evidence is “confounded” with fiber/bran (e.g. observational research historically included products with 25% bran content as whole grain)

- Expanded analysis converts conclusions for CVD from inconclusive to strongly positive

- Diabetes is inconclusive for either analysis

- Because of nutrient variability among whole grains, the beneficial health effects of one whole grain may not be the same for other whole grains
Study participants

- LSRO
  - Fabiana DeMoura, Ph.D.
  - Kara Lewis, Ph.D.
  - Michael Falk, Ph.D.

- Expert Panel
  - James Hoadley, Ph.D.
  - Julie Mares, M.S.P.H, Ph.D
  - Judith Marlett, R.D., Ph.D.
  - Harry Sapirstein, Ph.D.
The LSRO Report and Beyond

- Implications for national nutrition advisory bodies
  - US Dietary Guidelines Advisory Committee

- Implications for health claims
  - Accuracy
  - Applicability to all grains
  - Difficulty in quantification of ingredients
  - Reconsideration of FDAMA whole grain claims to include fiber/bran/germ components
  - Considerations by EFSA for Article 14 claims
Thank you for your consideration

Michael Falk, Ph.D.
301-634-7030
301-634-7876 (fax)
Falkm@LSRO.org