

Citation:

De Moura FF, Lewis KD, Falk MC. Applying the FDA definition of whole grains to the evidence for cardiovascular disease health claims. *J Nutr*. 2009 Nov; 139 (11): 2,220S-2,226S.

PubMed ID: [19776180](#)

Study Design:

Meta-analysis or Systematic Review

Class:

M - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To evaluate the effect of applying the US Food and Drug Administration (FDA) definition of whole grains to the strength of scientific evidence in support of claims for risk reduction of cardiovascular disease (CVD).

Inclusion Criteria:

- Human intervention and observational studies
- Studies that measured a validated end-point (i.e., coronary heart disease, myocardial infarction, ischemic heart disease and stroke) or surrogate endpoints (i.e., blood pressure, total cholesterol concentration, and serum LDL-cholesterol) for cardiovascular disease in a healthy US population and populations representative of the US
- The restricted analysis included only studies that explicitly described or defined grains according to the FDA definition of whole grains. (The FDA defines whole grains as consisting of the "intact, ground, cracked or flaked fruit of the grains whose principal components—the starchy endosperm, germ and bran—are present in the same relative proportions as they exist in intact grain")
- The expanded analysis included studies with a broader definition of whole grains, including studies that added bran or germ along with whole grains or studies that did not explicitly use the term whole grains, but were in fact were conducted with individual whole grains.

Exclusion Criteria:

- Reviews, editorials and meta-analysis studies
- Animal and in vitro studies.

Description of Study Protocol:

Recruitment

- A search of the scientific literature was conducted by searching MEDLINE for articles published through February 2008 using the following search strategy: (whole grain OR whole grains) AND (cardiovascular disease OR heart OR coronary heart disease OR stroke OR blood pressure OR myocardial infarction OR health OR diabetes)
- Additional articles were identified from a Web of Science database using the same keywords used for the MEDLINE search
- Other studies were identified by bibliographic searched of relevant reviews and articles.

Design

Systematic review.

Dietary Intake/Dietary Assessment Methodology

Not applicable.

Blinding Used

Two scientists independently reviewed each article for inclusion and to ensure that the information was accurately abstracted from the article.

Intervention

Not applicable.

Statistical Analysis

Not applicable.

Data Collection Summary:

There was great variation among the studies regarding variables and measures.

Description of Actual Data Sample:

- *Initial N*: The MEDLINE searches returned 634 potentially relevant articles
- *Attrition (final N)*:
 - Four studies (two observational and two intervention) conformed to the FDA definition of whole grains and were included in the restricted analysis
 - The expanded analysis included a total of 29 studies (15 intervention and 14 observational)
- *Age*: Not specified
- *Ethnicity*: Not specified
- *Other relevant demographics*: Healthy US populations and populations representative of the US
- *Anthropometrics*: None
- *Location*: Most studies were conducted in the US (one each in China, Iran, Sweden, England, Germany and Japan).

Summary of Results:

Key Findings

- Restricted analysis using FDA definition of whole grains: Although two observational studies found a significant reduction of CVD-related surrogate end-points, the absence of support from intervention studies leads to the conclusion that there is not enough evidence to support a health claim for the reduced risk of CVD
 - One prospective cohort study observed a reduced relative risk of coronary heart disease comparing the highest to the lowest quintile of whole grain intake (P for trend=0.01)
 - One cross-sectional study observed a decrease in total cholesterol of 0.16mmol/L comparing the highest to the lowest quintile of whole grain intake (P for trend=0.02)
 - Two randomized, crossover design intervention studies did not observe any significant differences compared to controls when evaluating surrogate endpoints such as total cholesterol, LDL-cholesterol and blood pressure
- Expanded analysis: A whole grain and cardiovascular disease health claim is supported using a broader concept of whole grain typically used in the scientific literature that includes whole grain foods containing principal components such as bran
 - The results of the 14 observational studies included in the expanded definition, regardless of their whole grain source, suggested a protective association between whole grain intake and risk of CVD
 - A beneficial effect of oats on CVD outcomes was reported in six studies (four with a significant (P<0.05) positive effect), whereas one study showed no effect. The positive studies were also conducted for a longer time period (six to eight weeks vs. three weeks)
 - Four intervention studies with barley showed reduction in plasma total cholesterol (20-15%) and LDL-cholesterol (21%) levels. The positive effect of barley reported across population, gender, and health status adds strength to the evidence for a beneficial health effect of barley on plasma total cholesterol and LDL-cholesterol levels.

Other Findings

- Health benefits observed from the consumption of one whole grain do not necessarily reflect the same benefit or the same magnitude of benefit from other whole grains
- Among the intervention studies included in the expanded definition, only the studies conducted with oats and barley reported reduced cholesterol levels.

Author Conclusion:

When considering only whole grain studies that met the FDA definition, there was insufficient scientific evidence to support a claim that whole grain intake reduces the risk of cardiovascular disease. However, a whole grain and reduced risk of cardiovascular disease is supported when using a broader concept of whole grain to include studies that considered intake of fiber-rich bran and germ as well as whole grain.

Reviewer Comments:

Study Strengths

- *Two scientists independently reviewed each article for inclusion and to ensure the information was accurately abstracted*
- *Included studies measured a validated end-point or surrogate endpoint for coronary heart disease.*

Study Limitations

- *Trials of individual whole grains, such as oats and rye, were put in the expanded definition group, although it was clear that these met the FDA definition by design*
- *Surrogate outcomes for intervention studies were presented as "significant" with a P-value or not significant, rather than providing estimates and confidence intervals*
- *Review limitations are not described*
- *Potential reasons for differences in individual study results are not well described.*

Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions

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|----|---|-----|
| 1. | Will the answer if true, have a direct bearing on the health of patients? | Yes |
| 2. | Is the outcome or topic something that patients/clients/population groups would care about? | Yes |
| 3. | Is the problem addressed in the review one that is relevant to nutrition or dietetics practice? | Yes |
| 4. | Will the information, if true, require a change in practice? | Yes |

Validity Questions

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|----|--|-----|
| 1. | Was the question for the review clearly focused and appropriate? | Yes |
| 2. | Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search terms used described? | Yes |
| 3. | Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased? | Yes |
| 4. | Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible? | No |
| 5. | Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined? | Yes |
| 6. | Was the outcome of interest clearly indicated? Were other potential harms and benefits considered? | Yes |

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| 7. | Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issues considered? If data from studies were aggregated for meta-analysis, was the procedure described? | Yes |
| 8. | Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included? | Yes |
| 9. | Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed? | No |
| 10. | Was bias due to the review's funding or sponsorship unlikely? | Yes |