Whole-grain intake and cancer: an expanded review and meta-analysis

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Authors' objectives
To investigate the association between whole-grain intake and the risk of cancer.

Searching
The authors searched MEDLINE from 1984 to 1997, and selected articles based on the occurrence of 'whole grain', 'whole meal' or 'cancer' in the title or abstract. They also scanned studies that mentioned 'diet' and 'cancer'. Additional studies were by reviewing references in retrieved papers, and by searching for articles written by any of the principal investigators of groups who have published case-control studies of cancer.

Case-control studies from an earlier review by the same authors were also included in this review (see Other Publications of Related Interest).

Study selection
Study designs of evaluations included in the review
Retrospective case-control studies assessing the dietary intakes of patients with cancers or colon polyps versus those of non-cancer controls.

Specific interventions included in the review
Various types of whole-grain intake were described in the studies: brown bread, crisp bread, high-fibre cereal, nonwhite bread, whole grains, whole-grain bread, whole-grain bread and cereal, whole-grain bread and pasta, whole-grain cereal, whole-grain foods, whole-grain pasta, and wholemeal bread.

Participants included in the review
People with various types of cancer or colon polyps, and hospital, visitor or population controls. The types of cancers considered were pancreatic, gastric, colorectal, colon, rectal, endometrial, breast, soft-tissue sarcoma, non-Hodgkin's lymphoma, ovarian, Hodgkin's disease, myelomas, brain, colorectal polyps and oral, including pharynx, tongue, liver, oesophageal, prostate, thyroid, bladder and larynx. The average age of the participants in the studies ranged from 18 to 80 years.

Outcomes assessed in the review
The risk of developing cancer was assessed, based on a high versus low intake of whole-grain food. The various types of cancer considered were pancreatic, gastric, colorectal, colon, rectal, endometrial, breast, soft-tissue sarcoma, non-Hodgkin's lymphoma, ovarian, Hodgkin's disease, myelomas, brain, colorectal polyps and oral, including pharynx, tongue, liver, oesophageal, prostate, thyroid, bladder and larynx cancers. The participants were assessed on their consumption of certain foods prior to the onset of disease using dietary questionnaires and interviews.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed quality.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.
Methods of synthesis

How were the studies combined?
The authors computed the total number of incidences of whole-grain intake and the number of incidences in which the odds ratio (OR) was less than 1. They also computed the number of incidences in which the original article indicated that the comparison of risk in high versus low intake of whole grain achieved statistical significance.

The overall pooled ORs, weighted by the inverse of the study variance, were then calculated along with 95% confidence intervals (CIs); within-category ORs were also calculated.

Dose response associations were studied by computing pooled ORs within dosage levels. Significance levels were assessed by regressing ORs in their respective dosage levels in repeated measures, weighting inverse to the variance.

How were differences between studies investigated?
Pooled ORs were calculated both within- and between-studies.

The authors also assessed whether the decreased ORs for cancer observed with a high intake of whole grains might be explained by confounding. Study variables including age, gender, race, education, location, certain food consumption, life-style, family medical history, social status and others were adjusted for in the individual case-control studies.

Results of the review

Forty case-control studies with a total of 43,708 participants (14,658 in the cancer groups and 29,050 in the control groups) were included.

In the 40 case-control studies, high versus low intake of whole-grain foods gave an OR of less than 1 in 46 of the 51 (90%) incidences, with 28 of the 51 (55%) individually achieving conventional statistical significance.

When 6 incidences with possible design or reporting flaws or low intake of whole grain were omitted, 43 of the 45 (96%) incidences had ORs of less than 1, with 26 of the 45 (58%) achieving statistical significance.

The pooled OR was 0.69 (95% CI: 0.61, 0.77) for all 51 incidences, 0.66 (95% CI: 0.60, 0.72) for the 45 incidences, and 1.14 (95% CI: 0.71, 1.57) for the 6 excluded incidences. The pooled ORs according to type of cancer were within the range 0.5 to 0.8 with the exceptions of breast (0.86) and prostate (0.9) cancers (the CIs were not stated).

A dose-response relationship was seen in the 26 studies of frequency of eating: the pooled OR was 0.82 in the occasional eaters and 0.59 in the habitual eaters of whole grain (the CIs were not stated).

Authors' conclusions

The case-control evidence was supportive of the hypothesis that whole-grain intake protects against various cancers. The authors state that the findings of the present review, taken together with known beneficial action of many nutrients contained in whole grains and the possibility of synergistic action of nutrients packaged in their natural form, suggest that it would be prudent for the public to eat more whole-grain foods.

CRD commentary

The authors stated the review question, inclusion criteria, study details and methodology for pooling in a comparison of the available literature. They made a competent search of the literature, including case-control studies from their previous review (see Other Publications of Related Interest).

The authors searched the literature but did not stated whether any language restrictions were applied, or whether non-Western studies were found or excluded. This may have resulted in relevant material being missed.

The authors stated the inclusion criteria and study design, but did not describe how decisions to include studies were made, or on what basis the included studies were judged to be relevant. There was also no quality review of the
included studies.

The studies used in the review were all case-control designs which are retrospective and open to recall bias by participants. The questionnaires and interviews of participants were not uniform and there was heterogeneity between the included studies in terms of depth of questionnaires, adjustment variables used, and control groups (some hospital-based versus population-based). In addition, the included studies focused on European and American populations and diet.

The conclusions in this review should be viewed with caution since the included trials are retrospective (and possibly open to recall bias), have not been reviewed for quality, and should not be generalised to other populations with different dietary intakes.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that it would be desirable to conduct clinical trials of whole-grain intake and cancer prevention to fully assess confounding as an explanation of the findings of this review, but this may not be feasible due to the required size, cost and duration of such trials. A study of the biological effects of whole grain and its constituents is more feasible and should be pursued vigorously.

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