Effects of omega-3 fatty acids on cancer risk: a systematic review

CRD summary
This well-conducted review assessed the effects of omega-3 fatty acids on cancer risk. The authors concluded that there is no evidence to suggest that there is a significant association between omega-3 fatty acids and cancer incidence. The authors' conclusions are likely to be reliable.

Authors' objectives
To assess the effects of omega-3 fatty acids on cancer risk.

Searching
This report is an update of one section of a larger systematic review (see Other Publications of Related Interest). The original search was performed on MEDLINE, EMBASE and CAB Health from the inception of the databases to October 2003. PREMEDLINE and the Cochrane CENTRAL Register were searched in October 2003. An updated search was performed in October 2005. Letters were sent to industry experts to obtain any unpublished data. The search terms were reported and no language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Prospective cohort studies that evaluated whether omega-3 fatty acids reduce tumour incidence were eligible. Case-control studies were excluded from the review.

Specific interventions included in the review
Studies that described exposure to omega-3 fatty acids appear to have been eligible for inclusion, although no explicit details of the inclusion criteria were provided. The included studies assessed the effects of omega-3 fatty acids overall and considered the specific effects of consuming fish, marine omega-3 fatty acids, and alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) individually.

Participants included in the review
Studies that included human participants were eligible for inclusion in the review; no further details were provided. There was a wide variety of participants in the studies: Caucasian, black and Asian participants with birth years ranging from 1880 to 1974. Both males and females with a wide range of cancers were included.

Outcomes assessed in the review
Studies that included a description of the effects of omega-3 fatty acids on tumour incidence were eligible for inclusion; no further details were provided. The studies included in the review reported tumour incidence for eleven types of cancer, with over half reporting on breast, colorectal or prostate cancer.

How were decisions on the relevance of primary studies made?
Two reviewers independently evaluated the titles and abstracts of primary studies. Any disagreements were resolved through consensus.

Assessment of study quality
Information relating to the ascertainment of cases and exposure, description of withdrawals and drop-outs, adjustment for confounders, and blinded assessment of exposure and case status of the included observational studies was recorded. No scores of quality were calculated. Two reviewers independently extracted data on the quality of the included studies.
Data extraction
Two reviewers independently abstracted the data onto a detailed summary table. Any differences were resolved through consensus, with disagreements referred to a third reviewer. For each of the studies, the multivariate-adjusted risk ratios (RRs) reported for the group with the highest reported intake of omega-3 fatty acids relative to the group with the lowest reported intake of omega-3 fatty acids were presented.

Methods of synthesis
How were the studies combined?
The studies were presented in a narrative synthesis, owing to heterogeneity between the identified studies.

How were differences between studies investigated?
Plots of the point estimates of the RRs weighted according to the inverse of the variance were produced in order to assess the possible effects of sample size. The study results were presented according to type of cancer and were discussed in terms of type of omega-3 fatty acid.

Results of the review
Twenty different cohort studies were identified. These ranged in size from 6,000 to 121,000 participants with 9,000 to 1.5 million person-years of observation, with a total of over 700,000 participants and 3 million person-years of observation.

All of the included cohort studies were of variable quality. Qualitative and visual evaluation suggests that there were no differences in reported risks based on sample size.

Breast cancer (8 studies, n=412,134): one study found that there was an increased risk of breast cancer for women in the highest quartile of fish consumption compared with women in the lowest quartile (incidence RR 1.47, 95% confidence interval, CI: 1.10, 1.98). Two studies found that there was a reduced risk for women consuming larger amounts of fish or marine omega-3 than for women with lower consumption: the RRs were 0.77 (95% CI: 0.60, 0.98) and 0.72 (95% CI: 0.53, 0.98), respectively. None of the other studies found associations between breast cancer and omega-3 consumption. One study reported a reduced risk of breast cancer for women in the highest quintile of ALA consumption compared with women in the lowest quintile (RR 0.70, 95% CI: 0.51, 0.97), but no associations between EPA or DHA consumption and breast cancer risk.

Colorectal cancer (9 studies (7 cohorts), n=391,376): one study suggested that there was a reduced risk of colorectal cancer for those in the highest quartile of fish intake compared with those in the lowest quartile (RR 0.49, 95% CI: 0.27, 0.89). One study suggested a trend for a reduction in risk for those with higher consumption of omega-3 when adjusting for age. None of the other studies demonstrated associations between colorectal cancer risk and omega-3 consumption.

Lung cancer (n=151,987): of the 3 studies that evaluated the relationship between lung cancer and omega-3 intake through fish consumption, one suggested an increased risk of lung cancer (incidence RR 3.0, 95% CI: 1.2, 7.3), one suggested a reduced risk of lung cancer (RR 0.32, 95% CI: 0.13, 0.76), and the third showed no association.

Prostate cancer (7 studies (5 cohorts), at least n=129,255): one study found that there was a reduced risk of prostate cancer for men that never or seldom ate fish compared with those with moderate consumption (RR 2.3, 95% CI: 1.2, 4.5), one study showed a trend towards a similar effect, and two found no association. One study reported an increased risk of prostate cancer for men in the highest quintile of ALA consumption compared with men in the lowest quintile (RR 1.98, 95% CI: 1.34, 2.93). No association was found between prostate cancer risk and EPA, DHA or marine omega-3 consumption in the same study.

Skin cancer (n=64,779): one study was identified. This demonstrated an increase in the risk of basal cell carcinoma for those in the highest quartile of omega-3 fat consumption compared with those in the lowest quartile of consumption (RR 1.13, 95% CI: 1.01, 1.27).

No significant associations between omega-3 fatty acids and cancer risk were found with regards to aerodigestive
cancer (n=8,006), bladder cancer (n=8,006), lymphoma (n=163,537), ovarian cancer (n=183,163), pancreatic cancer (n=148,811) or stomach cancer (n=13,250).

**Authors’ conclusions**
There was no evidence to suggest that there is a significant association between omega-3 fatty acids and cancer incidence.

**CRD commentary**
The review question was generally broad and clear in terms of the participants, outcomes and study designs eligible for inclusion in the review; however it was not well defined in terms of eligible interventions. Several databases were searched, without language restrictions, and some attempts were made to locate unpublished literature; this reduces the possibility of publication or language bias. The study selection, data extraction and quality assessment processes were carried out in duplicate, which minimises the possibilities of reviewer bias or error. The use of a narrative synthesis was entirely appropriate given the differences in the studies included in the review. This was a well-conducted review and the authors’ conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that dietary supplementation with omega-3 fatty acids is unlikely to prevent cancer.

Research: The authors did not state any implications for future research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.