

POSITION STATEMENT

Omega-3 fatty acids, fish and cancer prevention



Key messages

Omega-3 (n-3) fatty acids (FAs) are associated with a range of health benefits. Oily fish such as swordfish, atlantic salmon, gemfish and spanish mackerel, are rich sources of n-3 FAs.

There is *limited suggestive* evidence for an association between increased fish consumption and a reduced risk of breast, colorectal and prostate cancer; and between a higher n-3 to omega-6 (n-6) FA ratio in the diet and a reduced risk of breast cancer. The evidence for an inverse association between n-3 FAs and cancer risk is largely insufficient to draw any meaningful conclusions. The available research studies are too limited in number, consistency and quality to permit a conclusion of a probable or definite link between n-3 FAs and a reduction in cancer risk.

The scientific evidence for a range of health conditions clearly supports people including n-3 FAs from both marine and plant sources as part of a balanced diet. n-3 FAs are known to help reduce the risk of heart disease, lower triglycerides and relieve inflammatory conditions such as rheumatoid arthritis and inflammatory bowel disease.

Therefore Cancer Council recommends people:

- Eat fish (preferably oily) at least two times per week
- Include some plant foods and oils rich in n-3 FAs in their diet.

These recommendations are consistent with those made by Heart Foundations around the world and the Dietary Guidelines for Australian Adults.

Cancer Council encourages all people to follow the recommendations of the Foods Standards Australia and New Zealand (FSANZ) about consumption of fish high in mercury.

Cancer Council supports further research in order to improve knowledge on the benefit of n-3 FAs, fish and cancer risk and the underlying mechanisms involved.

Rationale

Omega-3 (n-3) fatty acids (FAs) are associated with a range of health benefits, particularly for heart disease and inflammatory conditions like arthritis. Emerging evidence from both experimental and epidemiological studies suggests n-3 FAs may play a role in cancer prevention.¹ Therefore it is important for the Cancer Council to evaluate the effects of n-3 FAs and fish in relation to cancer.

Background

Types of n-3 FAs

Polyunsaturated fatty acids include the n-3 and omega-6 (n-6) FA families. n-3 FAs are characterised by having their first double bond in the n-3 position i.e. at the third carbon from the methyl end of the molecule.

The main fatty acids in this group are α -linolenic acid (ALA), and the long chain fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). ALA is an essential fatty acid for humans, as it is required for normal function and the body is unable to make it and must obtain it from the diet.² A small amount of EPA and DHA can be formed in the body from ALA, however most are acquired directly from dietary sources.

Food Sources of n-3 FAs

Generally speaking, plant foods contain ALA and marine animals provide EPA and DHA.³ Foods that naturally contain high levels of ALA include canola oil, soybean oil, flaxseed/linseed oil and walnut oil. The best natural dietary sources of EPA and DHA include oily fish such as swordfish, atlantic salmon, gemfish and spanish mackerel, as well as oysters. Meats such as beef, chicken and lamb contain smaller amounts of n-3 FAs.

However the distinction is becoming less clear as the food chain is manipulated. For example common foods such as milk, bread and eggs are being transformed into functional foods that provide significant amounts of n-3 FAs, a role that they have not played previously. Fish oil supplements that contain large quantities of EPA and DHA are also readily available for consumption. Therefore n-3 FAs may now be obtained from a wide range of different sources.

n-6 FAs are found in plant based foods and some animal tissues. Main food sources of n-6 FAs include corn, safflower, sunflower, sesame, peanut, soybean and cottonseed oils, as well as walnuts.

Functions of n-3 FAs

n-3 FAs play a structural role in cell membranes. EPA incorporated into cell membranes can act as a precursor to a variety of eicosanoids and cytokines that can have widespread effects on the human body. Eicosanoids are a group of hormone like substances and include thromboxanes, prostaglandins, and leukotrienes.

It is important to note that n-6 FAs compete with n-3 FAs for incorporation into the cell membrane, and when the n-6 FA, arachidonic acid, is present it gives rise to a different set of eicosanoids.⁴ These eicosanoids include stronger platelet aggregators and inflammatory mediators.^{2,4} Therefore the ratio of n-3:n-6 FAs present in the membrane is highly important for determining the types of eicosanoids produced.^{1,5,6}

The ability of n-3 FAs to promote an anti-inflammatory state in the human body is also related to the production of cytokines. Cytokines such as tumour necrosis factor α , interleukin-1 and interleukin-6 act to initiate an inflammatory reaction when released by the immune system. The n-3 FAs are known to weaken this process by reducing the production of cytokines.^{4,7}

Views on n-3 FAs and fish in cancer prevention reports

In 2007, the World Cancer Research Fund and the American Institute of Cancer Research (WCRF) found there was *limited suggestive* evidence that fish intake reduced the risk of colorectal cancer.⁸ No conclusions were made for other cancers or n-3 FAs, however WCRF noted the biological plausibility of n-3 FAs in fish for the protection of cancer.⁸

Prior to this, the World Health Organization (WHO) reported that there was *possible / insufficient* evidence for an association between n-3 FAs, fish and reduced cancer risk,⁹ and the United Kingdom Department of Health's Committee on the Medical Aspects of Food and Nutrition Policy (COMA) reported that there was insufficient evidence to draw a conclusion for fish intake.¹⁰

Epidemiology evidence

Because of the lack of detail given to n-3 FAs and fish intake in major cancer prevention reports, Cancer Council NSW conducted a systematic literature review and meta-analysis in 2006 of studies that investigated the intake of n-3 FAs and fish in relation to cancer risk.¹¹ The review found that the available literature in this area was lacking in consistency and quantity, which meant that it was difficult to make definitive conclusions.

Table 1 shows the conclusions from the review on the association between n-3 FAs, fish and risk of cancer (breast, colorectum and prostate), using the WCRF classifications for levels of evidence.⁸ Pooled results for studies included in the review can be seen in the appendix.

Table 1. Summary of conclusions on n-3 FAs and fish by cancer site in Cancer Council NSW systematic literature review.¹¹

Cancer	Type of n-3 fatty acid	Classification of evidence, using WCRF definitions
Breast	Fish, n-3:n-6	Limited (suggestive evidence): decreased risk
	Total n-3, long chain n-3, ALA, EPA, DHA	Limited evidence (no conclusion)
Colorectal	Fish, total n-3, long chain n-3, ALA, EPA, DHA, n-6:n-3	Limited evidence (no conclusion)
Colon	Fish, total n-3, ALA, EPA, DHA, n-3:n-6	Limited evidence (no conclusion)
Rectal	Fish	Limited (suggestive evidence): decreased risk
	ALA, EPA, DHA	Limited evidence (no conclusion)
	Total n-3, n-6:n-3	No relevant studies identified
Prostate	Fish	Limited (suggestive evidence): decreased risk
	ALA	Limited (suggestive evidence): increased risk
	Total n-3, long chain n-3, EPA, DHA, linoleic acid:ALA (marker of n-6:n-3 ratio)	Limited evidence (no conclusion)

A higher fish intake appears to be associated with a slightly decreased risk of breast, rectal and prostate cancer. There were very few studies available which examined the association between n-3 FAs and other cancer types.¹² Therefore it was not possible to reach any conclusions on the relationship between n-3 FAs and other cancers.¹²

Interestingly, the European Prospective Investigation into Cancer (EPIC) Study found that a high intake ($\geq 80\text{g/day}$) of fish (which included fresh, canned, salted and smoked fish) was associated with a significant decrease in the risk of colorectal and rectal cancers, but no association was found for colon cancer on its own.¹³ This study was released after the literature search was completed for the systematic review and so was not included in the pooled analysis. It adds to the evidence that rectal and possibly colorectal cancer incidence may be reduced with a high fish intake.

No consistent pattern was observed for all cancers when the results from countries with high fish consumption were examined separately in the review. This suggests that people in countries with a relatively high consumption of fish do not necessarily have an advantage when it comes to reducing cancer risk. It could be that the benefits of consuming fish plateau after a certain level. Ideally studies in populations with a wide variation in intake of fish are required to definitively answer the question.

Interestingly, no association was seen for the specific long chain n-3 FAs, EPA or DHA, which are the n-3 FAs found in fish. This finding is inconsistent with the evidence from experimental studies in animals which show that long chain n-3 FAs can suppress the growth of cancer cells.¹⁴⁻¹⁶ Inconsistencies between results for specific fatty acids and fish may be due to some extent to the difficulties in calculating intake of fatty acids. Although fish may vary in n-3 FA content, and this is not likely to be well captured by a typical FFQ, the measurement of fish intake will probably be more accurate than the estimate of n-3 FA intake, which also relies on the detailed information of other sources of fatty acids.

In contrast to the other results for n-3 FA intake, the review found that ALA may be associated with an increased risk of prostate cancer. ALA is an essential fatty acid as the body is unable to synthesise it, and is found mostly in plant-based oils. An explanation for the suggestive relationship between ALA and increased prostate cancer risk is unknown at this stage. Other researchers have postulated that it may have something to do with confounding by other dietary factors, but this doesn't appear to be the case.^{17,18} It is a plausible argument however, as ALA is commonly obtained from a variety of foods including fats, oils, meats and poultry.¹⁹ Hence the association may have more to do with the particular food source of ALA, rather than the specific FA.

Recommendations to limit ALA in the diet because of the suggestive relationship with prostate cancer risk are not warranted at this point in time, as conclusive evidence is lacking. What's more, ALA has not been associated with an increased risk for any other cancers. In addition, ALA has been shown to reduce the risk of heart disease and this benefit is likely to balance or outweigh the possible risks to the prostate.¹⁸

The results on FA ratios suggest that more n-3 FAs and less n-6 FAs in the diet (and therefore in the cell membrane) may protect against breast and possibly even colorectal cancer. Hence it could be the case that the results for total n-3 FA, long chain n-3 FA and the individual n-3 FAs were not showing statistical significance in the included studies because they were evaluated at an absolute level, not in a ratio to the n-6 FAs. However, this theory does not account for the fact that some studies found fish intake was protective against cancer of the breast, rectum and prostate, despite the fact that fish species were not reported and could have been quite low in n-3 FA content. Further research on n-3 FAs, the ratio of n-3 to n-6 FAs and fish intake is needed, notwithstanding the complexity of measuring the dietary intake of specific fatty acids.

Potential mechanisms of action

Experimental studies (including animal and in vitro studies) have shown that n-3 FAs have multiple mechanisms as cancer chemopreventive agents.^{1,6,20} Potential mechanisms of action of n-3 FAs include:

- Inhibition of eicosanoid production from n-6 FA precursors (arachidonic acid) which leads to suppression of neoplastic transformation; cell growth inhibition; enhanced apoptosis; and anti-angiogenesis^{1,5,6}
- Alteration of oestrogen metabolism which leads to reduced oestrogen-stimulated cell growth.⁶

Recommendations

There is a growing body of scientific evidence that dietary intake of n-3 FAs and fish could be beneficial in reducing the risk of some cancers. More scientific research is required to improve our understanding of the extent of this benefit and the underlying mechanisms involved. The scientific evidence on n-3 FAs for other health conditions, besides cancer, clearly supports people including n-3 FA from both marine and plant sources as part of a balanced diet. n-3 FAs are known to help reduce the risk of heart disease, lower triglycerides and relieve inflammatory conditions such as rheumatoid arthritis and inflammatory bowel disease.

Cancer Council supports the National Health and Medical Research Council adequate intake level of 0.8g/day for women and 1.3g/day for men in relation to ALA intake, and the adequate intake level of 90mg/day for women and 160mg/day for men, with an upper intake limit of 3000mg/day, in relation to total long chain n-3 intake.²¹

Cancer Council also supports the National Health and Medical Research Council suggested dietary target of 430mg/day for women and 610mg/day for men in relation to long chain n-3 intake, in order to reduce the risk of chronic disease.²¹

Cancer Council Australia recommends people:

- Eat fish (preferably oily) at least two times per week
- Include some plant foods and oils rich in n-3 FAs in their diet.

These recommendations are consistent with those made by Heart Foundations around the world and the Dietary Guidelines for Australian Adults.²²

Consumption patterns in Australia

Many Australian adults currently consume far less than the recommended level of long chain n-3 FAs in order to reduce the risk of chronic disease.¹⁹ The primary food source of EPA and DHA in the Australian diet is fish and seafood, as would be expected. However meat and poultry consumption also greatly contribute to the intake of these n-3 FAs, due to the large amount that is eaten. ALA is obtained primarily by eating cereal-based products, fats and oils and meat and poultry.

Australian fish species that are oily include swordfish, atlantic salmon, gemfish and spanish mackerel, while canned species high in n-3 FA content include sardines, mackerel, salmon and tuna.²³⁻²⁶ A list of fresh and canned fish species found in Australia and their n-3 FA content is shown in table 2. Plant foods and oils rich in n-3 FAs include canola oil, canola margarine, soybeans, soybean oil, linseeds, linseed oil (flaxseed oil), walnuts, walnut oil and leafy vegetables.²⁷ Vegetarians need to ensure that they obtain adequate n-3 FAs via these plant sources.

Table 2. The omega-3 fatty acid (n-3 FA) content of fresh²³ and canned (packed in brine, water or spring water)²⁶ fish species found in Australia

Fish species	Fresh or canned	n-3 FA content (mg/100g)
Swordfish	Fresh	1059
Salmon, Atlantic	Fresh	689
Gemfish	Fresh	441
Mackerel, spanish	Fresh	411
Trout, rainbow	Fresh	309
Warehou, silver	Fresh	308
Dory, silver	Fresh	303
Mullet, sea	Fresh	299
Snapper	Fresh	223
Redfish	Fresh	194
Dory, john	Fresh	188
Perch, brownband sea	Fresh	167
Bream, yellowfin	Fresh	146
Mullet, yelloweye	Fresh	133
Perch, reef ocean	Fresh	119
Tuna, yellowfin	Fresh	117
Snapper, goldband	Fresh	114
Ling, pink	Fresh	113
Flathead, marbled	Fresh	99
Barramundi, salt water	Fresh	98
Barramundi, fresh water	Fresh	89
Sardine	Canned	2837 - 4044
Mackerel	Canned	1409 - 3570
Salmon	Canned	497 - 2738
Tuna	Canned	177 - 370

It is important to note that some fish species can contain high levels of mercury.²⁸ Mercury accumulates in the aquatic food chain as methylmercury, and is known to damage the nervous system at high levels.²⁹ Therefore eating fish that contain high levels of mercury every day or in large quantities could be harmful. Mercury is known to easily cross the blood brain barrier and the placenta,³⁰ which means that a foetus can also be exposed to high concentrations of mercury.

Therefore advice on mercury in fish is particularly important for children, and women that are pregnant or intending to become pregnant.²⁹ Food Standards Australia New Zealand (FSANZ) have developed a set of recommendations on the number of serves of different types of fish that can be safely consumed by the Australian population (table 3). Cancer Council encourages all people to follow these recommendations when eating fish.

Table 3. FSANZ recommendations for consumption of fish species high in mercury²⁹

Population	Serve size	Recommendations
Children	1 serve equals 75g	2-3 serves per week of any fish and seafood not listed below OR 1 serve per week of Orange Roughy (Deep Sea Perch) or Catfish and no other fish that week OR 1 serve per fortnight of Shark (Flake) or Billfish (Swordfish/Broadbill and Marlin) and no other fish that fortnight
Pregnant women/women intending to become pregnant	1 serve equals 150g	
Rest of the population	1 serve equals 150g	2-3 serves per week of any fish or seafood not listed below OR 1 serve per week of Shark (Flake) or Billfish (Swordfish/Broadbill and Marlin) and no other fish that week

Fish oil supplements may be useful if dietary fish intake is low³¹ and foods fortified with n-3 FA such as milk and bread may also be used to supplement n-3 FA intake.³² However, the use of fish oil supplements should be done in conjunction with the advice of a health care professional. Potential side effects include gastrointestinal upset, increased bleeding time and increased cholesterol.³¹ In addition, some fish oil supplements include vitamin A and D, which can be toxic at high doses.

Although the evidence for a link between the n-3 FA and n-6 FA ratio and cancer risk is largely insufficient to draw conclusions at this stage, it is well known that the modern diet is much higher in n-6 FAs and lower in n-3 FAs than that of our ancestors.³³ It is also well known that n-6 FA intake can impact greatly on n-3 FA uptake in the body. Considering there is some evidence that more n-3 FA and less n-6 FA in the diet may be associated with a reduced risk of breast cancer, eating patterns that improve the n-3 FA and n-6 FA ratio should be encouraged.

Practical and healthy ways to increase the intake of n-3 FAs in the diet include:

- Have grilled or steamed n-3 FA rich fish with vegetables for dinner
- Mix canned n-3 FA rich fish through a salad or put on a sandwich with salad
- Use n-3 FA rich fish and other seafood in mixed dishes such as curries, stews, casseroles, pastas and soups
- Use canned n-3 FA rich fish to make fish cakes and serve with vegetables
- Make a homemade seafood pizza
- Use canola oil in cooking
- Use canola based margarines on breads
- Eat soy and linseed bread
- Use linseeds when making homemade breads and savoury muffins
- Sprinkle linseeds over breakfast cereal
- Use whole soybeans in stews, casseroles and soups
- Blend soybeans and use in dips
- Eat a small handful of n-3 FA rich nuts such as walnuts as a snack
- Include n-3 FA rich nuts such as walnuts when making homemade breads, muffins and cakes
- Try baking apples or pears that have been stuffed with walnuts and sultanas
- Include green leafy vegetables such as broccoli, cabbage and spinach in mixed dishes like curries and stir fries
- Include green leafy vegetables in a salad
- Make a spinach pie

Future research

In the future, more studies need to be designed that are:

- Prospective i.e. randomised controlled trials and cohort studies
- Able to comprehensively measure and report n-3 FAs in the diet from all sources, including plant and animal species, supplements and functional foods
- Able to classify the n-3 FA group into individual fatty acids in order to investigate the association between specific fatty acids and risk of cancer
- Able to investigate the association between the n-3 to n-6 ratio and cancer risk
- Consistent in the way they measure or report data e.g. calculation of the n-3 to n-6 ratio and classification for levels of evidence
- Are performed in populations with sufficient variation in intake of fish and individual fatty acids.

Further information

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Acknowledgments

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Appendix

Breast cancer

Table 4 shows the pooled results for cohort and case-control studies of breast cancer from the Cancer Council NSW systematic literature review.¹¹ There appears to be no association between intake of n-3 FAs (including total n-3 FAs, long-chain n-3 FAs, ALA, EPA and DHA) and risk of breast cancer.

Table 4. Pooled results for cohort and case-control studies of breast cancer.¹¹

Exposure measured	Study type & number	Pooled odds ratio	Confidence interval	p-value*
Fish	Cohort (n=4)	1.01	0.83-1.24	0.01
Fish	Case-control (n=7)	0.82	0.71-0.96	0.05
Total n-3	Case-control (n=6)	0.75	0.48-1.16	0.08
Long chain n-3	Cohort (n=2)	0.84	0.68-1.04	0.19
Long chain n-3	Case-control (n=3)	0.95	0.44-2.06	0.06
ALA	Case-control (n=7)	0.98	0.57-1.69	<0.01
EPA	Case-control (n=4)	0.83	0.63-1.08	0.50
DHA	Case-control (n=6)	0.75	0.52-1.06	0.11

*Test for heterogeneity between studies in each group

The evidence suggests that fish intake is associated with a decreased risk of breast cancer. For fish intake, the pooled odds ratio from cohort studies (n=4) was 1.01 (95% CI 0.83-1.24), and from case-control studies (n=7) was 0.82 (95% CI 0.71-0.96). While cohort studies suggest that no association is present, case-control studies show that the risk is reduced when fish was consumed. Many of these studies show a significant trend ($p < 0.05$) of decreasing risk with higher levels of fish intake. The level of fish intake that was most associated with a decreased risk was approximately two to three or more serves per week.

The evidence also suggests that a higher n-3 to n-6 FA ratio (i.e. more n-3 FAs and less n-6 FAs in the diet) is associated with a decreased risk of breast cancer. The majority of studies that examined the relationship between n-3 and n-6 FAs found that a higher n-3 to n-6 FA ratio was associated with slight inverse association of breast cancer incidence. However the confidence intervals of these studies included the value of one, hence it was impossible to rule out no association between these factors. Furthermore, the majority of studies found that the trend was not significant ($p > 0.05$) when the n-3 to n-6 FA ratio increased. Nonetheless, two studies did find that a higher intake of n-3 to n-6 FAs was associated with a substantially reduced risk of breast cancer and the trend for this association was significant.^{34,35}

Menopausal status does not appear to have an impact on the association. One cohort study showed no association between fish intake and breast cancer risk for both pre and postmenopausal women.³⁶ The risk was reduced for postmenopausal women when compared to premenopausal women in two studies that examined fish and long chain n-3 FA intake.^{37,38} In contrast, another case-control study suggested that the risk associated with EPA and DHA intake is slightly less for premenopausal women.³⁴ However the confidence intervals for pre and post menopausal groups overlap in all studies, hence there is no significant effect modification of menopausal status.

Oestrogen receptor positive breast cancer was more strongly associated with total fish intake than oestrogen receptor negative breast cancer.³⁹ However the number of oestrogen receptor negative tumours was small and the authors were unable to postulate a reason for the result. Therefore further research is needed before a conclusion can be made on the influence of n-3 FAs on breast cancer type.

Colorectal cancer

Table 5 shows the pooled results for cohort and case-control studies of colorectal, colon and rectal cancers from the Cancer Council NSW systematic literature review.¹¹ The evidence is strongest for an association between fish intake and rectal cancer, compared with the other sites within the colorectum. There appears to be no association between intake of ALA, EPA and DHA and risk of colorectal, colon and rectal cancer. There also appears to be no association between total n-3 and long chain n-3 FA intake and risk of colorectal cancer and the intake of total n-3 FAs and risk of colon cancer.

Table 5. Pooled results for cohort and case-control studies of colorectal cancer.¹¹

Exposure measured	Cancer	Study type & number	Pooled odds ratio	Confidence interval	p-value*
Fish	Colorectal	Cohort (n=5)	0.95	0.71-1.28	0.06
Fish	Colorectal	Case-control (n=2)	0.99	0.49-2.03	0.01
Fish	Colon	Cohort (n=4)	0.95	0.66-1.39	0.21
Fish	Colon	Case-control (n=8)	0.86	0.63-1.17	<0.01
Fish	Rectal	Case-control (n=5)	0.68	0.48-0.96	0.02
Total n-3	Colon	Case-control (n=2)	0.95	0.78-1.17	0.58
Long chain n-3	Colorectal	Cohort (n=2)	0.90	0.48-1.68	0.08
EPA	Colorectal	Cohort (n=2)	0.91	0.71-1.15	0.47
EPA	Colon	Case-control (n=2)	1.02	0.81-1.27	0.26
DHA	Colorectal	Cohort (n=2)	0.96	0.75-1.22	0.47

*Test for heterogeneity between studies in each group

The evidence is suggestive that fish intake may be associated with a decreased risk of rectal cancer. For fish intake and rectal cancer risk, the pooled odds ratio for case-control studies (n=5) was 0.68 (95% CI 0.48-0.96). The amount of fish consumed (species mainly unspecified) in these studies ranged from two or more serves per week to four or more serves per week. No association was found between fish intake and colorectal or colon cancers.

The evidence indicates that a higher n-6 to n-3 FA ratio (i.e. more n-6 FAs and less n-3 FAs in the diet) might be associated with an increased risk of colorectal cancer. However there is only limited evidence on which to base this conclusion, as the studies that exist to date are lacking in quantity. Therefore no conclusion can be reached.

Prostate cancer

Table 6 shows the pooled results for cohort and case-control studies of prostate cancer from the Cancer Council NSW systematic literature review.¹¹ As for breast and colorectal cancer, there appears to be no association between intake of n-3 FAs (including total n-3 FAs, long-chain n-3 FAs, EPA and DHA) and risk of prostate cancer.

Table 6. Pooled results for cohort and case-control studies of prostate cancer.¹¹

Exposure measured	Study type & number	Pooled odds ratio	Confidence interval	p-value*
Fish	Cohort (n=2)	0.95	0.84-1.09	0.50
Fish	Case-control (n=4)	0.65	0.47-0.90	0.51
Total n-3	Case-control (n=2)	1.10	0.67-1.80	0.09
ALA	Case-control (n=6)	1.72	1.09-2.70	<0.01
EPA	Cohort (n=2)	0.90	0.79-1.02	0.46
EPA	Case-control (n=5)	0.92	0.63-1.34	0.16
DHA	Cohort (n=2)	0.91	0.80-1.04	0.41
DHA	Case-control (n=5)	0.90	0.66-1.23	0.35

*Test for heterogeneity between studies in each group

However the evidence is suggestive that fish intake may be associated with a decreased risk of prostate cancer. For fish intake and prostate cancer risk, the pooled odds ratio for cohort studies (n=2) was 0.95 (95% CI 0.84-1.09), and for case-control studies (n=4) was 0.65 (95% CI 0.47-0.90). The overall pattern for these studies is consistent. Even though two cohort studies indicate that a high fish intake is not associated with prostate cancer risk, the evidence from case-control studies shows that fish intake is linked with a decreased risk. Two of these studies also showed there was a significant trend ($p<0.05$) of decreasing risk with increased levels of fish intake.^{40,41} Furthermore, another case-control study indicated that when fish intake was reduced, the risk of prostate cancer increased.⁴² The level of fish intake (species mainly unspecified) associated with these results ranged greatly from one or more serves per week to seven or more serves per week.

In contrast to all other results for n-3 FA intake and prostate cancer risk, the evidence is suggestive that ALA may be associated with an increased risk of prostate cancer. The pooled odds ratio for case-control studies (n=6) and ALA intake was 1.72 (95% CI 1.09-2.70). The odds ratio for the only cohort study lies close to unity, however the majority of the case-control studies have odds ratios greater than one and show a significant trend ($p<0.05$) of increasing risk with higher levels of ALA intake.

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