

Position statement

Fish, fish oils, n-3 polyunsaturated fatty acids and cardiovascular health

This position statement was developed to provide recommendations to the general population and health professionals on the consumption of fish, fish oils and n-3 polyunsaturated fatty acids for cardiovascular health.

In addition, this statement provides cautions on the consumption of fish with high and medium methylmercury content.

The Heart Foundation advocates for change within the food industry and from governments.

Recommendations

The Heart Foundation makes the following recommendations with respect to fish, fish oils and omega-3 polyunsaturated fatty acids (n-3 PUFA) to improve the cardiovascular health of all Australians.

These recommendations are based on the evidence presented in the Heart Foundation's review of evidence *Fish, fish oils, n-3 polyunsaturated fatty acids and cardiovascular health*,^{1,2} as well as in our healthy eating guidelines. To view Heart Foundation guidelines and position statements, and a full reference list for this position statement, see www.heartfoundation.org.au/Professional_Information/Lifestyle_Risk/Nutrition.

Fish that live in cold water are rich in n-3 PUFA—particularly docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA). Alpha-linolenic acid (ALA) is a plant-based n-3 PUFA that has many health benefits but does not benefit cardiovascular health as well as marine n-3 PUFA.



Pregnant or breastfeeding women, women planning pregnancy, and children should:

1. Follow the recommendations for the adult Australian population.
2. Not exceed recommended doses of fish and fish oil supplements.
3. Follow the advice from Food Standards Australia and New Zealand on mercury in fish.

All adult Australians

To lower their risk of coronary heart disease (CHD), all Australians should:

1. Consume about 500 mg per day of combined DHA and EPA through a combination of the following:
 - two or three serves (150 g serve) of oily fish per week
 - fish oil capsules or liquid
 - food and drinks enriched with marine n-3 PUFA.
2. Consume at least 2 g per day of ALA.
3. Follow government advice on fish consumption regarding local safety issues.
4. Discuss healthy eating and concerns about nutrition with an Accredited Practising Dietitian or a doctor.

Health professionals

Health professionals should advise adult Australians with documented CHD to:

1. Consume about 1000 mg per day of combined DHA and EPA through a combination of the following:
 - two or three serves (150 g serve) of oily fish per week
 - fish oil capsules or liquid
 - food and drinks enriched with marine n-3 PUFA.
2. Consume at least 2 g per day of ALA.
3. Follow government advice on fish consumption regarding local safety issues.
4. Discuss healthy eating and concerns about nutrition with an Accredited Practising Dietitian or a doctor.

Health professionals should advise adult Australians with elevated triglycerides (TG) to take fish oil capsules or liquid and marine n-3 PUFA enriched foods and drink as first-line therapy by:

- starting with a dose of 1200 mg per day of DHA and EPA; and if appropriate
- increasing the dose to 4000 mg per day of DHA and EPA and checking their patient's response every 3 to 4 weeks when the dose is changed, until target TG levels are reached.

Governments

The Heart Foundation encourages governments to:

1. Recommend that Australians consume fish and fish oils.
2. Commit to collecting data on the Australian population's dietary intake (including of n-3 PUFA) through a regular national nutrition survey.
3. Include fish oil capsules and liquid in the Pharmaceutical Benefits Scheme to help health professionals to prescribe them to people who have CHD.
4. Support professional development for doctors that includes advice on fish and fish oil consumption for those with, and at risk of, CHD.
5. Support sustainable fishing practices and healthy, sustainable marine ecosystems.
6. Monitor levels of methylmercury and dioxins in Australian fish.

The food industry

To encourage the consumption of fish and fish oils by the Australian population, the food industry should:

1. Develop a variety of foods that are enriched with n-3 PUFA.
2. Promote fish and seafood that come from sustainable sources.
3. Retain marine oils where possible during the processing of fish and seafood.

Rationale

The consumption of fish, fish oils and n-3 PUFA is associated with a reduced risk of cardiovascular disease (CVD).^{3,4} However, since the Heart Foundation's report *Review of the relationship between dietary fat and cardiovascular disease*³ in 1999 new findings have been published in Australia and internationally regarding the benefits of, and cautions about consuming n-3 PUFA.

The World Health Organization recommends an intake of 1–2 servings of fish (where each serving is defined as providing 200–500 mg/week DHA and EPA) as protective against CHD and stroke.⁴ In 2006 the National Health and Medical Research Council (NHMRC) issued *Nutrient Reference Values for Australia and New Zealand Including Recommended Dietary Intakes*,⁵ which recommended an intake of combined DHA, EPA and DPA of 610 mg/day for men and 430 mg/day for women to prevent chronic disease.

To consolidate the extensive literature on fish, fish oils and n-3 PUFA, and to explore the international recommendations regarding their cardiovascular health benefits, a literature review was conducted on behalf of the Heart Foundation by Associate Professor David Colquhoun* and Antonio Ferreira-Jardim†.

* School of Medicine, University of Queensland, Greenslopes and Wesley Hospitals, Brisbane, Australia
† University of Queensland, Core Research Group, Brisbane, Australia

Further information

To view Heart Foundation guidelines and position statements see www.heartfoundation.org.au.

The review aimed to:

- determine the extent of the association between the consumption of fish, fish oils and n-3 PUFA and the reduction in CHD mortality
- determine the extent of the association between the consumption of fish, fish oils and n-3 PUFA and serum TG levels
- derive population-based recommendations for the consumption of fish, fish oils and n-3 PUFA to lower the risk of CHD and in the secondary prevention of CHD
- identify possible toxic risks associated with fish and fish oil consumption.

The findings and the levels of evidence of the scientific literature discussed in the Heart Foundation's review of evidence *Fish, fish oils, n-3 polyunsaturated fatty acids and cardiovascular health*,⁶ are summarised below.

Summary of evidence

Evidence	Level of evidence
Individuals with a higher intake of fish have a lower risk of CHD mortality, total CHD and total stroke. ⁷⁻⁹	III-2
Consuming fish at least once a week is associated with a lower risk of total stroke and CHD mortality in the general population and in post-myocardial infarction patients. ⁷⁻¹¹	III-2
In secondary prevention, a diet with 2 g/day of ALA decreases the risk of CHD. ¹²⁻¹⁴	II
In secondary prevention, ≥ 850 mg/day marine n-3 PUFA supplementation reduces the risk of CHD mortality and ≥1,800 mg/day reduces major coronary events. ¹⁵⁻¹⁷	II
In secondary prevention, there is conflicting evidence about the effects of marine n-3 PUFA supplementation on the risk of sudden death in patients. ^{15,18-22}	n/a
Marine n-3 PUFA supplementation of 1000–4000 mg/day decreases serum TG levels by 25–30% and increases high-density lipoprotein (HDL) cholesterol levels by 1–3%. A dose relationship exists between intake of marine n-3 PUFA and decreased serum TG levels. ²³⁻²⁵	I
Marine n-3 PUFA has an additive effect to statin therapy in decreasing serum TG levels and increasing HDL cholesterol. ²⁶⁻³²	II
Consuming fish with high levels of methylmercury may result in long-term neurological damage. Gestational exposure to methylmercury may result in neurodevelopmental deficits. ³²	III-3
The consumption of oily fish twice a week promotes cardiovascular health without excessive exposure to mercury. ^{34,35}	III-1
There is inconclusive evidence to support a relationship between mercury exposure and the incidence of CVD. ³⁶	n/a
Fish oil capsules available in Australia have zero or near zero methylmercury content. ³⁷	IV
Fish oil capsules in Australia contain very low levels of dioxins (polychlorinated biphenyl (PCB)). ³⁸	IV

* See Rating of the evidence, page 7

Australian recommendations

The average n-3 PUFA intake of Australians has been estimated at 246 mg/day comprising 75, 71 and 100 mg/day from EPA, DPA and DHA respectively.³⁹ Seafood is by far the richest source of n-3 PUFA in the diet.

The NHMRC has recently published Nutrient Reference Values, which include recommendations for intake of ALA, DHA, EPA and DPA for the first time.⁵ Adequate intake values were set as follows:

- ALA: 1.3 g/day for men and 0.8 g/day for women
- DHA+EPA+DPA: 160 mg/day for men and 90 mg/day for women.

An upper limit for children, adolescents and adults was set at 3000 mg/day for DHA, EPA and DPA. No upper limit was set for ALA because there is no known level at which adverse effects occur.

To prevent chronic disease, dietary intakes for DHA, EPA and DPA have been set at the current 90th centile in the population, values that are known to be safe and to provide potential benefit.^{40,41} The suggested dietary target to reduce chronic disease is 610 mg/day for men and 430 mg/day for women.

Mechanisms of action

Fish and fish oils are thought to decrease the risk of CHD through several possible mechanisms, including:

- altering the lipid composition of cell membranes
- decreasing blood levels of TG
- increasing the level of HDL
- decreasing heart rate variability and heart rate
- increasing the threshold for ventricular fibrillation
- anti-platelet effects that decrease the risk of thrombosis
- improving endothelial function
- decreasing some inflammatory responses
- lowering blood pressure
- decreasing plasma leptin levels.

Fatty acids, particularly marine n-3 PUFA, are incorporated into cell membranes, and increasing the amount of PUFA in the membrane increases its fluidity and deformability.^{42,44} There is a dose-response relationship between intake of marine n-3 PUFA and reduction in blood TG level.²⁴ The higher the baseline TG level, the greater the response. In individuals with extremely high TG levels, n-3 PUFA supplementation may lower TG level by 50%.²³

Intake of marine n-3 PUFA is positively correlated with HDL levels. Animal and in vitro studies show that intake of marine n-3 PUFA increases the number of receptors for, and turnover of, HDL.^{45,46} Marine n-3 PUFA significantly decreases chylomicron levels and size, which improves their clearance.⁴⁷ Supplementation does not appear to alter the levels of total cholesterol or low-density lipoprotein (LDL) if the TG level is not high.²³

Marine n-3 PUFA modulates the activities of several enzymes involved in carbohydrate and lipid metabolism.^{48,49} These changes lead to decreased TG synthesis^{50,51} and increased mitochondrial beta-oxidation,⁵²⁻⁵⁴ with a subsequent decrease in the formation of very LDL cholesterol.^{55,56}

Marine n-3 PUFA have an additive effect when combined with lipid-lowering medication such as statins. Combined treatment decreases TG level,^{28,32} increases HDL level,^{29,30,57} and redistributes LDL particle size to a less dense (less atherogenic) form beyond the response to statin only.^{26,27}

Marine n-3 PUFA supplementation inhibits nuclear transcription factor κ B, a key transcription factor in cytokine gene expression, cellular adhesion and inflammation. Supplementation decreases cytokine and nitric oxide production by macrophages,^{58,59} and release of inflammatory markers and cytokines in response to mitogenic and inflammatory stimuli.⁶⁰

Elevated plasma leptin level is independently associated with CVD risk.⁶¹⁻⁶³ Marine n-3 PUFA supplementation inhibits leptin gene expression in an animal model,⁶⁴ and a diet rich in fish and marine n-3 PUFA is associated with low plasma leptin level independent of body fat content.⁶⁵ Marine n-3 PUFA has a mild anti-platelet effect but does not affect bleeding time.

Future research

The Heart Foundation recommends further research in the following areas:

- Large, high quality randomised controlled trials that measure the cardiovascular outcomes in individuals given dietary advice to increase their consumption of marine n-3 PUFA. These trials need long-term follow-up.
- Exploration of the Omega-3 Index (the percentage of EPA and DHA in red blood cells), which is considered an emerging risk factor.
- Human trials to quantify the effect of high-dose marine n-3 PUFA on heart rate variability.
- High-quality randomised controlled trials that measure the benefits of ALA on cardiovascular health. It is not clear whether ALA prevents recurrent coronary events although there are trends suggesting that this may be the case.



Terminology

ALA	Alpha-linolenic acid, n-3 fatty acid with 18-carbon chain, C18:3n-3
CHD	Coronary heart disease
CVD	Cardiovascular disease
DHA	Docosahexaenoic acid, n-3 fatty acid with 22-carbon chain, C22:6n-3
DPA	Docosapentaenoic acid, n-3 fatty acid with 22-carbon chain, C22:5n-3
EPA	Eicosapentaenoic acid, n-3 fatty acid with 20-carbon chain, C20:5n-3
Fish oil	Oil derived from fish rich in EPA and DHA
HDL	High-density lipoprotein cholesterol
LDL	Low-density lipoprotein cholesterol
Marine n-3 PUFA	Combination of EPA, DHA and DPA
n-3 PUFA	Omega-3 polyunsaturated fatty acid
PCB	Polychlorinated biphenyl
TG	Triglycerides

Rating of the evidence

Evidence is graded according to the NHMRC guidelines.⁶⁶

Levels of evidence for clinical interventions

Level of evidence	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies with concurrent controls and non-randomised allocation, cohort studies, case-control studies, or interrupted time series with a control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.
IV	Evidence obtained from case series, either post-test or pre-test and post-test.



For heart health information
1300 36 27 87
www.heartfoundation.org.au

Visit www.heartfoundation.org.au/Professional_Information/Lifestyle_Risk/Nutrition for:

- the full reference list for this position statement
- the full review of evidence *Fish, fish oils, n-3 polyunsaturated fatty acids and cardiovascular health*
- Q&As about fish oil
- fish recipe sheets
- fish eating plans
- a table of recommended fish and seafood and their omega-3 content.

© 2008 National Heart Foundation of Australia ABN 98 008 419 761
PRO-055

Disclaimer: This position statement has been developed by the Heart Foundation for general information. The statements and recommendations it contains are, unless labelled as 'expert opinion', based on independent review of the available evidence. While care has been taken in preparing the content of this material, the Heart Foundation and its employees cannot accept any liability, including for any loss or damage, resulting from the reliance on the content, or for its accuracy, currency and completeness.

This material may be found in third parties' programs or materials (including but not limited to show bags or advertising kits). This does not imply an endorsement or recommendation by the Heart Foundation for such third parties' organisations, products or services, including these parties' materials or information. Any use of Heart Foundation material by another person or organisation is done so at the user's own risk.

The information contained in this position statement is current as of June 2007.