

COCHRANE CORNER

Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease

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Background. Cardiovascular diseases (CVDs) are defined as conditions involving decreased blood flow to the heart that can lead to heart attacks, stroke or other disorders. CVDs are a common cause of death in low- and middle-income countries. In South Africa (SA) in particular, CVD is the leading cause of death after HIV/AIDS, responsible for 1 in 6 deaths. CVD risk factors include unhealthy diets, hypertension, obesity, high cholesterol levels and diabetes. Omega-3 fatty acids may have a protective role in the risk of developing heart disease.

Objectives. To evaluate the consequences of an increased intake of fish and plant-based omega-3 fatty acids on the risk of CVD mortality and events.

Methods. The inclusion criteria for this review were randomised controlled trials (RCTs) lasting at least 12 months, which investigated men and women aged ≥ 18 years. These participants had to be at any risk of CVD while receiving dietary supplements and an advised diet to promote the intake of omega-3. This diet included oily fish, fish oils and seeds rich in omega-3. Comparisons with the interventions included the participants' usual diet, no advice, no supplements, placebo or lower-dose omega-3. The review evaluated the effectiveness of these interventions on primary (e.g. CVD deaths and events), secondary (e.g. major adverse cerebrovascular or CVD events, body weight and other adiposity measures, and lipids) and tertiary (e.g. blood pressure and side-effects) outcomes.

Results. Evidence from this review indicates that increasing the intake of long-chain omega-3 fatty acids (LCn3) or alpha-linolenic acid (ALA) probably has little or no effect on all-cause CVD or coronary heart disease mortality. Evidence was of moderate certainty, except for all-cause mortality, where there was a high certainty.

Conclusions. According to moderate- to high-certainty evidence, short-chain fatty acids and LCn3 have little or no effect on mortality or cardiovascular health. However, omega-3 ALA slightly reduces the risk of CVD events and arrhythmias.

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Cardiovascular diseases (CVDs) are conditions involving decreased blood flow to the heart or congested blood vessels, which can lead to heart attacks, stroke or other disorders.^[1] CVDs are a recurrent cause of death in low- and middle-income countries.^[2] In South Africa (SA) in particular, CVD is the leading cause of death after HIV/AIDS, responsible for 1 in 6 deaths.^[3] CVD risk factors include unhealthy diets, hypertension, obesity, high cholesterol levels and diabetes.^[3,4] Omega-3 fatty acids (Table 1) may have a protective role in the risk of developing heart disease through its effects on CVD risk factors, such as lowering blood pressure, altering lipid profiles, improving vascular endothelial function and insulin sensitivity.^[1]

Objectives

This review aimed to assess the effects of increased intake of fish and plant-based omega-3 fatty acids on the risk of all-cause and CVD mortality, CVD events, adiposity and lipids. It also aimed to assess the protective role of omega-3 fatty acids in individuals at low and high risk of heart disease, at different doses and from different sources of omega-3 (e.g. dietary or supplemental).

Intervention and methods

This review included randomised controlled trials (RCTs) lasting at least 12 months, with men and women ≥ 18 years of age at any risk of CVD, where dietary supplements, a provided diet or advice on

diet was implemented to promote intake of omega-3. This included promoting the intake of specific foods, such as fish oils from oily fish and seeds rich in omega-3. These interventions were compared with the participants' usual diet, no advice, no supplementation, placebo or lower-dose omega-3. The review assessed the effects of these interventions on primary (e.g. CVD deaths and events), secondary (e.g. major adverse cerebrovascular or CVD events, body weight and other adiposity measures, and lipids) and tertiary (e.g. blood pressure and side-effects) outcomes.

A comprehensive search was conducted in CENTRAL, MEDLINE and EMBASE databases, as well as in two trial registers, to identify eligible studies. Study selection, data extraction and risk of bias assessment were independently conducted by two reviewers. Random-effects meta-analyses for primary outcomes were conducted separately for long-chain omega-3s (LCn3s) and alpha-linolenic acids (ALAs). Authors also used meta-regression to explore the effects of intervention dose, duration and others on primary outcomes, and followed standard Cochrane methodology.

Results

This review included 79 RCTs with 112 059 participants at varying CVD risk, mainly conducted in high-income countries. Most studies assessed supplementation with LCn3, but some studies assessed LCn3 or ALA-rich or ALA-enriched food or dietary advice.

Table 1. Omega-3 fatty acids

Types	Source	Food source
ALA	Plant oils	Pumpkin seeds, soybean, tofu
EPA	Marine oils	Fish oil, salmon, cod liver
DHA	Marine oils	Salmon, tuna, oysters

ALA = alpha-linolenic acid; EPA = eicosapentaenoic acid; DHA = docosahexaenoic acid.

Effects on mortality

Evidence indicates that increasing the intake of LCn3 or ALA probably has little or no effect on all-cause, CVD or coronary heart disease (CHD) mortality. Evidence was of moderate certainty, except for all-cause mortality, where there was a high certainty.

Effects on cardiovascular disease events

High LCn3 intake probably has little or no effect on CVD or CHD events, stroke or arrhythmias. Most evidence was of moderate certainty, except for CVD events, where it was of high certainty. Increased ALA intake makes little or no difference to CHD events, and its effects on stroke are unclear; however, it may slightly reduce the risk of CVD events (low-certainty evidence) and probably reduces the risk of arrhythmias (moderate-certainty evidence).

Effects on harms

The effect of LCn3 intake on bleeding, pulmonary embolus or deep-vein thrombosis is unclear, as the evidence is of very low certainty.

Conclusions

We concluded that, according to moderate- to high-certainty evidence, short-chain omega-3 fatty acids and LCn3 have little or no effect on mortality or cardiovascular health, except for the potential effect of the omega-3 ALA of slightly reducing the risk of CVD events and arrhythmias.

Most of the evidence is from high-income countries, and it is unclear whether the effects would be the same in the SA context, where baseline intake of omega-3 may differ.

Implications for practice

Considering the findings of this review within the local context, it is concluded that long-term (12 - 72 months) supplementation of LCn3 should not be recommended for the prevention of all-cause mortality or cardiovascular events (high-quality evidence) or for the prevention of CHD deaths, CHD events, stroke and arrhythmias (moderate-quality evidence; more research warranted). Increasing ALA may slightly reduce the risk of CHD mortality, arrhythmias and CVD events (moderate-quality evidence). However, the effect is small and supplementation is not warranted.

Considering the dietary intake of these fatty acids, meta-analyses of prospective studies have illustrated that regular fish intake (1 - 2 times per week) or dietary patterns high in omega-3 fatty acids (e.g. the Mediterranean diet) are beneficial for the primary and secondary prevention of CHD.^[5] Furthermore, ALA is an essential nutrient and should be consumed as part of a mixed diet. Dietary guidelines for LCn3 include eating two portions of fish per week (one being oily fish) to provide 500 mg/day of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA),^[6] and to increase the intake of flax seeds, chia seeds, hemp seeds, walnuts, soybean and/or canola to ensure sufficient ALA intake. South Africans generally do not meet the basic dietary guidelines for ALA, EPA and DHA.^[6]

While this review focused on the effects of LCn3 and ALA, a healthy dietary pattern that consists of fruit and vegetables, nuts, whole grains and dietary fibre, together with sodium restriction and reduced intake of sugar and sugar-sweetened beverages,^[5] is important for the primary and secondary prevention and treatment of CVD. Furthermore, the relationship between the intake of omega-3 and omega-6 polyunsaturated fatty acids (PUFA) influences health outcomes. Replacing one dietary constituent (e.g. processed omega-6 PUFAs or refined carbohydrates) with another (e.g. LCn3), may have different effects on health outcomes than only adding LCn3 to an unhealthy diet.^[7] Strategies to address other unhealthy lifestyle habits, such as smoking, physical inactivity, high stress and harmful sleeping patterns, should be in place, together with appropriate weight management guidelines and antihypertensive and hyperlipidaemic medication before considering LCn3 supplementation.

Supplements and food sources of omega-3 fats are generally expensive in SA. Foods high in LCn3 and ALA provide many additional benefits, such as being sources of high-quality protein and minerals v. supplementation. Policy interventions should focus on ensuring that South Africans can consume foods as set out in basic dietary guidelines, and increasing the availability of fish, seeds and nuts at more affordable prices.

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