

# Implementing AHRQ Effective Health Care Reviews

*Helping Clinicians Make Better Treatment Choices*

## Omega-3 Fatty Acids and Cardiovascular Disease

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### Key Clinical Issue

What is the effect of omega-3 fatty acid supplementation on cardiovascular outcomes?

### Evidence-Based Answer

In patients with established cardiovascular disease or an increased risk of cardiovascular disease, omega-3 fatty acid supplementation has no effect on major adverse cardiac events, all-cause mortality, sudden cardiac death, coronary artery revascularization, or hypertension.<sup>1</sup> (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.)

### Practice Pointers

Omega-3 fatty acids, including eicosapentaenoic acid, docosahexaenoic acid, docosapentaenoic acid, and alpha-linolenic acid, are essential long-chain and very long-chain polyunsaturated fatty acids. They are found in fish and other seafood (marine oils), except for alpha-linolenic acid, which is found in walnuts, leafy green vegetables, and other oils. These omega-3 fatty acids have been made into supplements with claims of physiologic benefits, including inflammation

regulation.<sup>1</sup> Since the correlation between fish consumption and cardiovascular health was first identified, hundreds of studies have evaluated the effects of omega-3 fatty acids on cardiovascular outcomes. The American Heart Association has concluded that increased fish intake or use of omega-3 supplements is reasonable for the prevention of recurrent heart failure, recurrent coronary heart disease, and sudden cardiac death in patients with coronary heart disease.<sup>2</sup>

The number of Americans using dietary supplements is increasing. An analysis of data from the National Health and Nutrition Examination Survey found that the use of fish oil supplements increased from 1.3% to 12% between 1999 and 2012.<sup>3</sup> This Agency for Healthcare Research and Quality (AHRQ) review, which updates a 2004 systematic review, included 147 articles with 61 randomized controlled trials of relatively limited duration and 37 longitudinal observational studies from 2001 to 2015.<sup>4</sup> Studies that analyzed levels of fish consumption without quantification of omega-3 fatty acid intake were excluded.<sup>1</sup>

The review found a high strength of evidence that omega-3 fatty acid supplementation has

**The Agency** for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to produce evidence to improve health care and to make sure the evidence is understood and used. A key clinical question based on the AHRQ Effective Health Care Program systematic review of the literature is presented, followed by an evidence-based answer based upon the review. AHRQ's summary is accompanied by an interpretation by an *AFP* author that will help guide clinicians in making treatment decisions. For the full review, clinician summary, and consumer summary, go to <https://www.effectivehealthcare.ahrq.gov/topics/fatty-acids-cardiovascular-disease/clinician>.

**This series** is coordinated by Kenny Lin, MD, MPH, Deputy Editor.

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**CME** This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 565.

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## Dietary and Supplemented Marine Oil Omega-3 Fatty Acids: Effects on and Associations with Cardiovascular and Intermediate Outcomes

Omega-3 fatty acids (source)	Outcome	Key findings	Net change or RCT hazard ratio (95% confidence interval)	Number and type of studies	Strength of evidence
Marine oil: EPA + DHA ± DPA* (mainly supplements or supplemented food)	Major adverse cardiac events	No effect in RCTs No association in observational studies of total dietary intake Unclear association in observational studies of fatty acid biomarkers	0.96 (0.91 to 1.02)	10 RCTs 3 observational studies of total dietary intake 2 observational studies of fatty acid biomarkers	●●●
	All-cause death	No effect in RCTs No association in observational studies of total dietary intake	0.97 (0.92 to 1.03)	17 RCTs 3 observational studies of total dietary intake	●●●
	Sudden cardiac death	No effect in RCTs No association in observational studies of total dietary intake	1.04 (0.92 to 1.17)	9 RCTs 1 observational study of total dietary intake	●●●
	Coronary revascularization	No effect in RCTs No association in observational studies of total dietary intake	Not available	6 RCTs 1 observational study of total dietary intake	●●●
	Atrial fibrillation	No effect in RCTs Inconsistent findings in observational studies of total dietary intake	Not available	3 RCTs 3 observational studies of total dietary intake	●●○
	Blood pressure (systolic, diastolic)	No effect	Systolic: 0.1 mm Hg (-0.2 to 0.4) Diastolic: -0.2 mm Hg (-0.4 to 0.5)	29 RCTs	●●●
	Triglycerides	Decrease	-24 mg per dL (-31 to -18)	41 RCTs	●●●
	High-density lipoprotein cholesterol	Increase	0.9 mg per dL (0.2 to 1.6)	34 RCTs	●●●
	Low-density lipoprotein cholesterol	Increase	2.0 mg per dL (0.4 to 3.6)	39 RCTs	●●●
	Total cholesterol: high-density lipoprotein cholesterol ratio	Decrease	-0.2 (-0.3 to -0.1)	11 RCTs	●●●

### Strength of evidence scale

- **High:** High confidence that the evidence reflects the true effect. Further research is very unlikely to change the confidence in the estimate of effect.
- **Moderate:** Moderate confidence that the evidence reflects the true effect. Further research may change the confidence in the estimate of effect and may change the estimate.
- **Low:** Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
- **Insufficient:** Evidence either is unavailable or does not permit a conclusion

**Note:** Most RCTs involved evaluations of supplements.

DHA = docosahexaenoic acid; DPA = docosapentaenoic acid; EPA = eicosapentaenoic acid; RCT = randomized controlled trial.

\*-Studies that reported combined EPA and DHA were analyzed together with studies that reported combined EPA, DHA, and DPA.

Adapted from the Agency for Healthcare Research and Quality, Effective Health Care Program. Omega-3 fatty acids and cardiovascular disease: current state of the evidence. Clinician research summary. Rockville, Md.: Agency for Healthcare Research and Quality; July 2017. [https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/fatty-acids-cardiovascular-disease\\_clinician.pdf](https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/fatty-acids-cardiovascular-disease_clinician.pdf). Accessed February 19, 2017.

mixed effects on cholesterol levels, decreasing triglycerides, increasing high-density lipoprotein cholesterol and low-density lipoprotein cholesterol, and slightly decreasing total cholesterol (high-density lipoprotein cholesterol ratio).<sup>1</sup> A high strength of evidence suggested that there is no benefit of omega-3 fatty acid supplementation for prevention of major adverse cardiac events (hazard ratio = 0.96; 95% confidence interval, 0.91 to 1.02). A high strength of evidence also showed no benefit for all-cause death and sudden cardiac death. These findings are consistent with the results of another recent meta-analysis of 10 clinical trials including nearly 80,000 individuals.<sup>5</sup> The AHRQ review also concluded that there was no benefit of supplementation in patients with coronary revascularization and atrial fibrillation. For systolic and diastolic blood pressures, omega-3 fatty acid supplementation had no effects.<sup>1</sup>

Although omega-3 fatty acid supplementation affects several cholesterol measurements, there is strong evidence overall that in persons with cardiovascular disease or at increased risk of cardiovascular disease, supplementation does not affect patient-oriented outcomes, including major adverse cardiac events, all-cause death, sudden cardiac death, revascularization, or high blood pressure. Family physicians should not encourage patients to take these supplements to prevent heart disease. Instead, patients should be encouraged to eat a healthy, balanced diet,<sup>6</sup> which can include foods high in omega-3 fatty acids.

**Editor's Note:** *American Family Physician* SOR ratings are different from the AHRQ Strength of Evidence (SOE) ratings.

**The views** expressed in this article are those of the authors and do not reflect the policy or position of the U.S. Army Medical Department, Department of the Army, Department of Defense, or the U.S. government.

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