

Meta-analysis finds that omega-3 fatty acids improved cardiovascular outcomes

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For decades, there has been great interest in whether omega-3 fatty acids can lower rates of cardiovascular events. In 2018, results from the Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention

Trial (REDUCE-IT) were published in the *New England Journal of Medicine* and showed that a high dose of a purified ethyl ester of eicosapentaenoic acid (EPA) in patients at elevated cardiac risk significantly reduced cardiovascular events. Results from the trial led to US, Food and Drug Administration, Health Canada, and European Medicines Agency approval of the prescription drug icosapent ethyl for reducing cardiovascular risk in patients with elevated triglycerides, as well as updates to worldwide guidelines. But prior and subsequent studies of omega-3 fatty acid supplements that combine EPA and docosahexaenoic acid (DHA) have had mixed results.

Investigators from Brigham and Women's Hospital and elsewhere conducted a systematic review and meta-analysis of 38 randomized controlled trials of omega-3 fatty acids. Overall, they found that omega-3 fatty acids improved cardiovascular outcomes. Results, now published in *eClinical Medicine*, showed a significantly greater reduction in cardiovascular risk in studies of EPA alone rather than EPA+DHA supplements.

"REDUCE-IT has ushered in a new era in cardiovascular prevention," said senior author Deepak L. Bhatt, MD, MPH, the executive director of Interventional Cardiovascular Programs at the Brigham and lead investigator of the REDUCE-IT trial. "REDUCE-IT was the largest and most rigorous contemporary trial of EPA, but there have been other ones as well. Now, we can see that the totality of evidence supports a robust and consistent benefit of EPA."

Bhatt and colleagues performed a meta-analysis of 38 randomized clinical trials of omega-3 fatty acids, including trials of EPA monotherapy and EPA+DHA therapy. In total, these trials included more than 149,000 participants. They evaluated key cardiovascular outcomes, including cardiovascular mortality, non-fatal cardiovascular outcomes, bleeding, and atrial fibrillation. Overall, omega-3 fatty acids reduced

cardiovascular mortality and improved cardiovascular outcomes. The trials of EPA showed higher relative reductions in cardiovascular outcomes compared to those of EPA+DHA.

The researchers note that there are crucial biological differences between EPA and DHA—while both are considered omega-3 fatty acids, they have different chemical properties that influence their stability and strength of the effect that they can have on cholesterol molecules and cell membranes. No [trials](#) to date have studied the effects of DHA alone on cardiovascular outcomes.

"This meta-analysis provides reassurance about the role of omega-3 [fatty acids](#), specifically prescription EPA," said Bhatt. "It should encourage investigators to explore further the cardiovascular effects of EPA across different clinical settings."

More information: Khan SU et al. "Effect of Omega-3 Fatty Acids on Cardiovascular Outcomes: A Systematic Review and Meta-Analysis" *eClinical Medicine* [DOI: 10.1016/j.eclinm.2021.100997](https://doi.org/10.1016/j.eclinm.2021.100997)

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