



## Abstract

# Effects of Omega-3 Fatty Acid Supplementation on Revascularization and Major Cardiovascular Events: A Systematic Review and Meta-Analysis <sup>†</sup>

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**Abstract:** Background and Objectives: The clinical benefits of omega-3 fatty acid (FA) supplementation in preventing and treating cardiovascular disease remain controversial. The aim of this study was to investigate the effects of omega-3 FA administration on revascularization and adverse cardiovascular events including myocardial infarction, stroke, unstable angina, heart failure, and cardiovascular events/mortality using a meta-analytical approach. Methods: A comprehensive search of MEDLINE, Embase, Scopus, Web of Science, and Cochrane Library was performed throughout January 2023. Randomized controlled trials (RCTs) including at least 500 participants that compared the effects of omega-3 FA formulations (eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), or the combination) versus placebo or standard of care controls were considered eligible. Results: Our analysis included 17 RCTs that enrolled a total of 131,686 participants randomized to combined EPA + DHA ( $n = 52,498$ ), EPA alone ( $n = 13,415$ ), and control ( $n = 65,771$ ). Overall, omega-3 FA supplementation was associated with reduced risk of revascularization [RR 0.91, 95% CI 0.84–0.99;  $p_{het} = 0.0002$ ;  $I^2 = 69\%$ ;  $p = 0.02$ ] and myocardial infarction [0.89, 95% CI 0.80–0.98;  $p_{het} = 0.04$ ;  $I^2 = 45\%$ ;  $p = 0.02$ ] compared to controls, but had no significant effects on stroke, unstable angina, heart failure, or cardiovascular events/mortality. Comparing combined EPA + DHA with EPA, EPA alone was associated with a greater reduced risk of revascularization [0.76, 95% CI 0.63–0.94] and myocardial infarction [0.72, 95% CI 0.62–0.83], and a significantly reduced risk of stroke [0.72, 95% CI 0.55–0.95] and unstable angina [0.73, 95% CI 0.62–0.85]. No significant differences were observed according to EPA + DHA dose, EPA dose, and statin use. Conclusions: Omega-3 FA supplementation was associated with a reduced risk of revascularization and myocardial infarction compared with controls. The use of EPA alone appeared to be associated with even greater benefits, but further high-quality studies are needed to clarify the role of omega-3 FA supplementation in the primary and secondary prevention of cardiovascular disease.



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