



# Randomized, crossover, head-to-head comparison of EPA and DHA supplementation to reduce inflammation markers in men and women: the Comparing EPA to DHA Study<sup>1–3</sup>

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## ABSTRACT

**Background:** To date, most studies on the anti-inflammatory effects of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in humans have used a mixture of the 2 fatty acids in various forms and proportions.

**Objectives:** We compared the effects of EPA supplementation with those of DHA supplementation (re-esterified triacylglycerol; 90% pure) on inflammation markers (primary outcome) and blood lipids (secondary outcome) in men and women at risk of cardiovascular disease.

**Design:** In a double-blind, randomized, crossover, controlled study, healthy men ( $n = 48$ ) and women ( $n = 106$ ) with abdominal obesity and low-grade systemic inflammation consumed 3 g/d of the following supplements for periods of 10 wk: 1) EPA (2.7 g/d), 2) DHA (2.7 g/d), and 3) corn oil as a control with each supplementation separated by a 9-wk washout period. Primary analyses assessed the difference in cardiometabolic outcomes between EPA and DHA.

**Results:** Supplementation with DHA compared with supplementation with EPA led to a greater reduction in interleukin-18 (IL-18) ( $-7.0\% \pm 2.8\%$  compared with  $-0.5\% \pm 3.0\%$ , respectively;  $P = 0.01$ ) and a greater increase in adiponectin ( $3.1\% \pm 1.6\%$  compared with  $-1.2\% \pm 1.7\%$ , respectively;  $P < 0.001$ ). Between DHA and EPA, changes in CRP ( $-7.9\% \pm 5.0\%$  compared with  $-1.8\% \pm 6.5\%$ , respectively;  $P = 0.25$ ), IL-6 ( $-12.0\% \pm 7.0\%$  compared with  $-13.4\% \pm 7.0\%$ , respectively;  $P = 0.86$ ), and tumor necrosis factor- $\alpha$  ( $-14.8\% \pm 5.1\%$  compared with  $-7.6\% \pm 10.2\%$ , respectively;  $P = 0.63$ ) were NS. DHA compared with EPA led to more pronounced reductions in triglycerides ( $-13.3\% \pm 2.3\%$  compared with  $-11.9\% \pm 2.2\%$ , respectively;  $P = 0.005$ ) and the cholesterol:HDL-cholesterol ratio ( $-2.5\% \pm 1.3\%$  compared with  $0.3\% \pm 1.1\%$ , respectively;  $P = 0.006$ ) and greater increases in HDL cholesterol ( $7.6\% \pm 1.4\%$  compared with  $-0.7\% \pm 1.1\%$ , respectively;  $P < 0.0001$ ) and LDL cholesterol ( $6.9\% \pm 1.8\%$  compared with  $2.2\% \pm 1.6\%$ , respectively;  $P = 0.04$ ). The increase in LDL-cholesterol concentrations for DHA compared with EPA was significant in men but not in women ( $P$ -treatment  $\times$  sex interaction = 0.046).

**Conclusions:** DHA is more effective than EPA in modulating specific markers of inflammation as well as blood lipids. Additional studies are needed to determine the effect of a long-term DHA supplementation per se on cardiovascular disease risk. This trial

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**Keywords:** DHA, EPA, inflammation, men and women, randomized controlled trial, risk factors

## INTRODUCTION

Subclinical inflammation is recognized as a key etiologic factor in the development of atherosclerosis that leads to ischemic heart disease (IHD).<sup>8</sup> (1, 2). There is a growing body of literature that has suggested that long-chain  $\omega$ -3 (n-3) PUFAs (LCn-3PUFAs), primarily EPA (20:5n-3) and DHA (22:6n-3), may attenuate the proinflammatory state that is associated with obesity and metabolic syndrome (MetS) (3). In that regard, a number of mechanisms supporting the purported anti-inflammatory effects of LCn-3PUFAs have been proposed. These mechanisms include the inhibition of the proinflammatory nuclear transcription factor  $\kappa$ B in various

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<sup>2</sup> The Canadian Institutes for Health Research was not involved in designing the study; conducting the study; the collection, management, analysis, or interpretation of the data; or preparation and review of the manuscript before submission.

<sup>3</sup> Supplemental Tables 1–6 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://ajcn.nutrition.org>.

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<sup>8</sup> Abbreviations used: apoB, apolipoprotein B; CRP, C-reactive protein; CVD, cardiovascular disease; IHD, ischemic heart disease; ITT, intent to treat; LCn-3PUFA, long chain  $\omega$ -3 (n-3) PUFA; MetS, metabolic syndrome; RCT, randomized controlled trial.

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