‘A compelling story’: Meta-analysis supports omega-3s for heart disease reduction

By Stephen Daniells+ 03-Jan-2017

EPA and DHA omega-3s from food and supplements may reduce the risk of coronary heart disease (CHD), according to results of a new meta-analysis.

Data from 18 randomized clinical trials (RCTs) indicated that EPA and DHA were associated with a non-statistically significant 6% risk reduction in CHD among all populations, while the risk reduction increased to a statistically significant 18% when data from 16 prospective cohort studies was assessed.

The findings of the meta-analysis, published in the *Mayo Clinic Proceedings* , also indicated that among RCTs there was a statistically significant reduction in CHD risk in higher risk populations, including a 16% in those with high triglycerides and 14% in those with high LDL cholesterol.

“What makes this paper unique is that it looked at the effects of EPA and DHA on coronary heart disease specifically, which is an important nuance considering coronary heart disease accounts for half of all cardiovascular deaths in the US,” said Dr Dominik Alexander, lead author and Principal Epidemiologist for EpidStat.

“The 6% reduced risk among RCTs, coupled with an 18% risk reduction in prospective cohort studies – which tend to include more real-life dietary scenarios over longer periods – tell a compelling story about the importance of EPA and DHA omega-3s for cardiovascular health.”

“A most comprehensive quantitative assessment”

Commenting independently on the meta-analysis, Bruce Holub, PhD, University Professor Emeritus at the University of Guelph, told us that previous reviews and meta-analyses have indicated somewhat mixed results with respect to the potential benefits of EPA/DHA omega-3 fatty acid intakes when selected randomized controlled trials (RCTs) or prospective cohort studies were chosen for the evaluation of diverse vascular and less-defined coronary outcomes.

“The present systematic literature search provides a most comprehensive quantitative assessment of the effect of EPA/DHA intakes and supplementation on the specific risk of coronary heart disease (CHD). Interestingly, the reduced risk of adverse CHD risk associated with omega-3 fatty acid intakes was particularly apparent amongst those with traditional risk factors (elevated triglyceride and/or LDL-cholesterol levels),” said Prof Holub.

Pof Holub added that subsequent to the published literature coverage date used by Alexander et al, other studies have reported that higher blood levels of EPA/DHA are associated with lower cardiovascular mortality, higher EPA/DHA intakes offering protection from cardiac mortality, and reduced mortality and heart attacks after initial myocardial infarction with EPA/DHA supplementation, including, for example, Kleber et al., *Ather.*,252: 175-181 (2016) ; Sala-Vila et al., *J. Am. Heart Assoc.*, in press (2016) ; and Greene et al., *Am. J. Cardiol.*, 117: 340-346 (2016) .

Meta-analysis details

Dr Alexander and his co-workers analyzed data from with 93,000 and 732,000 subjects in 18 RCTs and 16 prospective cohort studies, respectively, and examined outcomes such as myocardial infarction, sudden cardiac death and coronary death.

Results showed that, while there was a non-statistically significant reduction in CHD risk with EPA+DHA for all participants of the RCTs, when the authors focused exclusively on higher-risk populations, including participants with elevated triglyceride and LDL cholesterol levels, a statistically significant CHD risk reduction with EPA+DHA was observed.

"Our results indicate that EPA+DHA provision reduced CHD risk among subjects with triglyceride levels of 150 mg/dL or more in RCTs but not among those with triglyceride levels within normal limits," wrote Dr Alexander and his co-authors. *"Similarly, a CHD risk reduction benefit of [omega- 3s EPA and DHA] provision was found among RCT subjects with low-density lipoprotein (LDL) cholesterol levels of 130 mg/dL or more but not for those with LDL cholesterol levels of less than 130 mg/dL.*

"These findings are particularly relevant for the management of CHD risk in the general US population because 25% of Americans older than 20 years are estimated to have triglyceride levels of 150 mg/dL or more and 27% of Americans aged between 40 and 74 years have LDL cholesterol levels of 130 mg/dL or more. Blood pressure is another well-documented CHD risk factor impacted favorably by n-3 LCPUFA administration."

"A simple, inexpensive, and achievable change"

The meta-analysis was funded by the Global Organization for EPA and DHA Omega-3s (GOED), but the organization played no role in any part of the analysis.

Commenting on the study's findings, Dr Harry Rice, GOED's VP of Regulatory and Scientific Affairs, said: *"There are important public health implications related*

to reducing the risk of coronary heart disease, and therefore we are encouraged by the results of this comprehensive analysis.

"It's also important that the observed risk reductions were even stronger in patient populations with elevated triglycerides and LDL cholesterol levels, two risk factors that affect more than one quarter of the American population."

Adam Ismail, GOED's Executive Director, added: *"The results confirm that increasing omega-3s is a healthy lifestyle intervention that can contribute towards reductions in CHD risk. "Remember that increasing omega-3 intakes is basically just improving the quality of one's diet slightly, like reducing the amount of sodium or increasing your dietary fiber. It is a simple, inexpensive, and achievable change that most consumers need to make to optimize their health."*

Adding oil to the engine

In an accompanying editorial, James O'Keefe, MD, and Dany Jacob, MD, from the University of Missouri–Kansas City, and Carl Lavie, MD, from the The University of Queensland School of Medicine in New Orleans, said that the analysis is the most comprehensive of its kind to date within the indexed biomedical literature.

"*Several large RCTs are currently under way that should help to clarify the issues surrounding the dosing and indications for omega-3 fatty acids. In the meantime, omega-3 fatty acid intake of at least 1 gram of EPA+DHA per day, either from seafood or supplementation (as recommended by the American Heart Association), continues to be a reasonable strategy,"* wrote Drs O'Keefe, Jacob, and Lavie.

"Nearly 30 years ago, Rogans wrote in the New England Journal of Medicine *that "fish oil is a whale of a story that not surprisingly gets bigger with each telling." The current article by Alexander et al adds oil to this engine."*

Source: *Mayo Clinic Proceedings*
January 2017, Volume 92, Issue 1, Pages 15–29, doi: 10.1016/j.mayocp.2016.10.018
"A Meta-Analysis of Randomized Controlled Trials and Prospective Cohort Studies of Eicosapentaenoic and Docosahexaenoic Long-Chain Omega-3 Fatty Acids and Coronary Heart Disease Risk"
Authors: D.D. Alexander et al.

Editorial: *Mayo Clinic Proceedings*
January 2017, Volume 92, Issue 1, Pages 1-3, doi: 10.1016/j.mayocp.2016.11.008 *"Omega-3 Fatty Acid Therapy: The Tide Turns for a Fish Story"*
Authors: J.H. O'Keefe, D. Jacob, C.J. Lavie