Public Health Implications of Recent Clinical Evidence on Omega-3 Fatty Acids and Cardiovascular Disease
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Please use the “questions” box on your “Go To Meetings” screen to submit questions to our presenters.

Please submit your questions at any time during today’s webinar.
Penny Kris-Etherton, PhD, RD, FAHA, FNLA, FASN, CLS  
*Distinguished Professor of Nutrition*  
*The Pennsylvania State University*

Ann Skulas-Ray, PhD  
*Assistant Professor, Department of Nutritional Sciences*  
*University of Arizona*

Patsy Brannon, PhD, RD  
*Professor, Department of Nutrition*  
*Cornell University*
Session #1: Making Sense of Omega-3 Headlines: Recent Evidence on Cardiovascular Outcomes and Public Health Implications (June 6)

Session #2: Public Health Implications of Recent Clinical Evidence on Omega-3 Fatty Acids and Cardiovascular Disease (June 23)

Summary of Session #1 Presentations

Penny M. Kris-Etherton PhD RD FAHA FNLA FASN
Evan Pugh University Professor of Nutritional Sciences
Distinguished Professor of Nutrition
Relevant Disclosures

• Seafood Nutrition Partnership - Member, Scientific Nutrition Advisory Council
Overview – Summary of:

Penny M. Kris-Etherton, PhD, RD, FAHA, FNLA, FASN, CLS - History of Omega-3 Recommendations in Cardiovascular Health and Disease

JoAnn E. Manson, MD, MPH, DrPH, FACP - How VITAL are Omega-3s for Heart Health? The VITAL Trial and Updated Meta-Analysis

Kevin C. Maki, PhD, CLS, FNLA, FTOS, FACN - Recent Clinical Evidence on EPA and DHA for CV Risk Reduction: Clinical Considerations

The FORCE Study – Exciting New Omega-3 Research
Three Updated AHA Science Advisories

• Siscovick DS et al. **Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation and the Prevention of Clinical Cardiovascular Disease**: A Science Advisory From the American Heart Association. Circulation. 2017;135:e867-e884.


Treatment is reasonable for:

- Secondary prevention of CHD and SCD among patients with prevalent CHD
- Secondary prevention of outcomes in patients with heart failure
Recommendation:

- 1 to 2 seafood meals per week to reduce risk of CHF, CHD, ischemic stroke and sudden cardiac death.
Main Points:

- When used to treat hypertriglyceridemia (200-499 mg/dL), n-3 FAs with EPA+DHA or with EPA-only appear roughly comparable for triglyceride lowering and do not increase LDL-C.

- In treatment of very high triglycerides (≥ 500 mg/dL) with 4 g/d, EPA+DHA agents reduce triglycerides by ≥30% with concurrent increases in LDL-C, whereas EPA-only did not raise LDL-C.
How *VITAL* are Omega-3s for Heart Health?  
*The VITAL Trial and Updated Meta-Analysis*

JoAnn E. Manson, MD, MPH, DrPH, FACP  
Professor of Medicine and the  
Michael and Lee Bell Professor of Women's Health  
Harvard Medical School  
Chief, Division of Preventive Medicine  
Brigham and Women's Hospital and Professor at  
Harvard T.H. Chan School of Public Health

*Nutrition 2020*  
*June 3, 2020*
Conclusions

• **VITAL Trial**

  • Omega-3s (1 g/d) supplementation did not significantly reduce the primary endpoint of major CVD events (or total cancer).

  • Omega-3s: ↓ Total MI by 28% (nominal p-value=0.003, adjusted p=0.015); greatest ↓ in those with low fish intake and in African Americans. PCI, fatal MI, total CHD were also ↓.

**UPDATED META-ANALYSIS**

• ↓ CHD/CVD with omega-3s, with dose-response gradient. (EPA may ↓ risk more than DHA.)
Recent Clinical Evidence on EPA and DHA for CV Risk Reduction: Clinical Considerations

Kevin C. Maki, PhD, CLS, FNLA, FTOS, FACN

Indiana University, Department of Applied Health Science, School of Public Health, Bloomington, IN & Midwest Biomedical Research, Addison, IL
Summary/Conclusions

• RCTs using low-dose (median 840 mg/d) EPA, or EPA and DHA, have produced mixed results, but, in total, support a small benefit (5-10%) for CHD risk, particularly fatal CHD
  – Evidence generally does not support a protective effect for stroke
  – Supplementation with long-chain omega-3 fatty acids is reasonable for CV health, especially for those who do not regularly consume oily fish (e.g., see VITAL)

• RCTs have shown significant benefits for higher-dosage EPA:
  – JELIS: 1.8 g/d EPA ethyl ester; 19% reduction in primary cardiac outcome vs. placebo; no benefit for stroke in primary prevention but a 20% risk reduction for stroke recurrence
  – REDUCE-IT: 4 g/d IPE (EPA ethyl ester) in subjects with elevated TG; 25% risk reduction in the primary outcome

• IPE is recommended by the NLA and other organizations for ASCVD risk reduction in select high- and very high-risk patients
  – The FDA approved an indication for IPE for ASCVD risk reduction for statin-treated patients with TG ≥150 mg/dL (only omega-3 agent with that indication)
CIRCULATING OMEGA-3 FATTY ACID LEVELS AND TOTAL AND CAUSE-SPECIFIC MORTALITY: PROSPECTIVE EVIDENCE FROM 16 COHORTS IN THE FATTY ACIDS AND OUTCOMES RESEARCH CONSORTIUM

Nathan Tintle, PhD
Professor of Statistics
Director of Kielstra Center for Research and Scholarship
Dordt University

Presented at the AHA Spring Epi-Lifestyle Meeting, Phoenix, AZ March 2020
### TABLE 2: ASSOCIATIONS OF OMEGA-3 FATTY ACIDS WITH RISK OF TOTAL AND CAUSE-SPECIFIC MORTALITY

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>All-cause mortality (16 cohorts)</th>
<th>CVD Mortality (14 cohorts)</th>
<th>Cancer Mortality (14 cohorts)</th>
<th>Other mortality (13 cohorts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALA</td>
<td>0.98 (0.94, 1.01)</td>
<td>1.00 (0.94, 1.06)</td>
<td>0.97 (0.91, 1.04)</td>
<td>0.99 (0.94, 1.05)</td>
</tr>
<tr>
<td>EPA</td>
<td>0.92 (0.89, 0.95)***</td>
<td>0.90 (0.84, 0.96)***</td>
<td>0.90 (0.85, 0.96)**</td>
<td>0.92 (0.87, 0.97)**</td>
</tr>
<tr>
<td>DPA</td>
<td>0.87 (0.83, 0.91)***</td>
<td>0.89 (0.82, 0.97)**</td>
<td>0.87 (0.80, 0.95)**</td>
<td>0.87 (0.81, 0.94)*****</td>
</tr>
<tr>
<td>DHA</td>
<td>0.89 (0.86, 0.93)***</td>
<td>0.88 (0.81, 0.95)**</td>
<td>0.93 (0.86, 1.01)</td>
<td>0.91 (0.85, 0.97)**</td>
</tr>
<tr>
<td>EPA+DHA</td>
<td>0.87 (0.84, 0.91)***</td>
<td>0.87 (0.80, 0.94)**</td>
<td>0.89 (0.82, 0.96)**</td>
<td>0.88 (0.82, 0.94)*****</td>
</tr>
</tbody>
</table>

Abbreviations: ALA, alpha-linolenic acid; CI, confidence interval; CVD, cardiovascular disease; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; and HR, hazard ratio.

Hazard ratio and confidence interval (CI) were expressed per a cohort-specific range of 10th to 90th percentile of each fatty acid.

*p<0.05, **p<0.01, ***p<0.001
Speakers

Ann Skulas-Ray, PhD – Department of Nutritional Sciences, University of Arizona, Tucson, AZ
Omega-3 Fatty Acids and Cardiovascular Disease: A Continuum of Nutrition and Medicine

Patsy Brannon, PhD, RD – Division of Nutritional Sciences, Cornell University, Ithaca, NY
The DRI Process - Considerations for Assessing Omega-3 Fatty Acids and Cardiovascular Disease in the DRI Framework of Chronic Disease Risk