

BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

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DYSLIPIDEMIA

Do omega-3 fatty acid supplements reduce CV risk?

Mounting evidence suggests they don't...despite prior evidence with Rx Vascepa (icosapent ethyl), a form of EPA (eicosapentaenoic acid).

Vascepa 2 g BID is approved to reduce CV risk in some high-risk patients with moderately elevated triglycerides despite statins.

Now evidence suggests that adding Rx Epanova 4 g/day for about 3 years does NOT improve CV outcomes in high-risk patients on statins.

Epanova is a combo of EPA and DHA (docosahexaenoic acid) that was approved in 2014 for severely high triglycerides over 500 mg/dL. But the company held its launch...while awaiting results of this CV trial.

Other new data show no CV benefit of a European omega-3 product with 1.8 g/day EPA and DHA after about 2 years in seniors with a recent heart attack.

Plus older studies with omega-3 doses of about 1 g/day are conflicting or suggest only slight benefit in some CV patients.

The contrasting data have researchers scratching their heads.

Some question if DHA negates the CV benefit of EPA. Or if Vascepa's results were inflated by the study's mineral oil placebo, which may have increased CV risk...possibly by reducing statin absorption.

For example, mineral oil raised LDL and high-sensitivity C-reactive protein. This wasn't seen with the Epanova study's corn oil placebo.

Educate that the CV benefits of omega-3s seem questionable... and all omega-3s may NOT have the same effects. Keep in mind, other Rx omega-3s (Lovaza) or fish oil supplements have both EPA and DHA.

Consider risks. Rx omega-3s are linked with increased risk of atrial fib...and omega-3 doses above 3 g/day may increase bleeding.

Plus Vascepa costs about \$330/month...its new generic is still \$300/month. Generic Lovaza costs about \$60/month.

Advise saving Rx omega-3s for patients with severely high triglycerides...to possibly reduce the risk of pancreatitis.

Don't rely on omega-3s for CV benefits. If needed, reinforce other measures...an optimized statin, BP control, smoking cessation, etc.

If a patient wants to use a fish oil supplement, encourage them to get one that's USP Verified. But point out that CV benefit isn't likely, no matter the dose or source (krill oil, etc).

Explore our chart, *Omega-3s: Fish Oil and More*, for guidance about dietary intake...and a deeper dive into the evidence.

(For more on this topic, see Clinical Resource #370105 at PharmacistsLetter.com.)

Nicholls SJ, Lincoff AM, Garcia M, et al. Effect of high-dose omega-3 fatty acids vs corn oil on major adverse cardiovascular events in patients at high cardiovascular risk: the STRENGTH randomized clinical trial. *JAMA* 2020;324:2268-80.

See LEADER NOTES for answers to discussion questions.

DISCUSSION QUESTIONS

OVERVIEW OF CURRENT THERAPY

1. What is known about the CV impacts of omega-3 fatty acids?

ANALYSIS OF NEW GUIDELINE

2. What type of study was this? How were the patients selected for inclusion?

3. How were the study groups defined?

4. How were the outcomes evaluated?

5. What were the outcomes of this trial?

See [LEADER NOTES](#) for answers to discussion questions.

6. What were the strengths and weaknesses of this trial?

7. Were the results expressed in terms we care about and can use?

HOW SHOULD THE NEW FINDINGS CHANGE CURRENT THERAPY?

8. Do the results change your practice? How?

APPLY THE NEW FINDINGS TO THE FOLLOWING CASE

JD is a 74-year-old male with a medical history of type 2 diabetes mellitus, tobacco abuse, hypertension, and hyperlipidemia who presents to the emergency department with left side chest pain. The ED work-up confirms a diagnosis of non-ST-elevation acute myocardial infarction. He is hospitalized and subsequently has a heart catheterization showing single vessel coronary artery disease with a 99% lesion of the right coronary artery that was treated with stent placement. His left anterior descending artery was diffusely calcified. An echocardiogram completed prior to discharge showed mild left ventricular hypertrophy with a normal left ventricular ejection fraction (EF) at 55-60%.

JD's condition is stabilized during his hospitalization. A few days later, he is preparing to be discharged.

See [LEADER NOTES](#) for answers to discussion questions.

9. What medications should JD be taking at time of hospital discharge for optimal management of his coronary artery disease (CAD)?

One week later, JD sees you in clinic for a hospital follow-up visit. He notes some fatigue but is otherwise doing well following discharge. He tells you that having a heart attack has been an eye-opening experience for him and he is ready to improve his overall health. A review of his medications shows he is taking metformin, metoprolol succinate, clopidogrel, lisinopril, aspirin, and atorvastatin. He asks you for recommendations to help prevent another heart attack. His sister recommended he take an omega-3 fatty acid or fish oil supplement and he asks your opinion.

10. What counsel do you provide JD on effects of omega-3 fatty acid supplementation on CV risk reduction?

You discuss the data regarding the CV impact of omega-3 supplements, and do not recommend starting an Rx product.

You counsel JD that if he opts to try a fish oil supplement, he should look for one that's USP Verified. However, you remind him that a reduction in overall CV risk is unlikely.

11. What lifestyle modifications do you suggest for JD that are shown to reduce his overall CV risk?

JD appreciates the recommendations and agrees to be referred to a tobacco cessation program. He also plans to begin a cardiac rehabilitation program in the near future. He agrees to work on dietary improvements and aim for overall weight loss. You schedule a follow-up visit with him in 3 months to re-evaluate his progress.

[See LEADER NOTES for answers to discussion questions.](#)

REFERENCES

Bhatt DL, Steg PG, Miller M, et al. Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. *N Engl J Med* 2019;380:11-22.

Curfman G. Do omega-3 fatty acids benefit health? *JAMA*;324:2280-1.

National Institutes of Health. Omega-3 fatty acids. Fact Sheet for Health Professionals. October 2020. <https://ods.od.nih.gov/factsheets/Omega3FattyAcids-HealthProfessional/>. (Accessed November 22, 2020).

Nicholls SJ, Lincoff AM, Garcia M, et al. Effect of high-dose omega-3 fatty acids vs corn oil on major adverse cardiovascular events in patients at high cardiovascular risk: the STRENGTH randomized clinical trial. *JAMA* 2020;324:2268-80.

Sharma G, Martin SS, Blumenthal RS. Effects of omega-3 fatty acids on major adverse cardiovascular events: what matters most: the drug, the dose, or the placebo? *JAMA* 2020;324:2262-4.

Siscovick DS, Barringer TA, Fretts AM, 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:e867-84.

Additional Pharmacist's Letter Resources available at [PharmacistsLetter.com](https://www.pharmacistsletter.com)

Chart, Omega-3s: Fish Oil and More. *Pharmacist's Letter/Prescriber's Letter*. January 2021.

Chart, Lipid Treatment FAQs. *Pharmacist's Letter/Prescriber's Letter*. January 2019.

Chart, Optimizing Care of Patients with Coronary Artery Disease. *Pharmacist's Letter/Prescriber's Letter*. February 2018.

Chart, Non-Statin Lipid-Lowering Agents. *Pharmacist's Letter/Prescriber's Letter*. March 2020.

Chart, Statin Dose Comparison. *Pharmacist's Letter/Prescriber's Letter*. April 2018.

Chart, Statin Muscle Symptoms: Managing Statin Intolerance. *Pharmacist's Letter/Prescriber's Letter*. June 2020.

Chart, Clinically Significant Statin Drug Interactions. *Pharmacist's Letter/Prescriber's Letter*. February 2016.

Chart, Common Cardiovascular Risk Calculators. *Pharmacist's Letter/Prescriber's Letter*. September 2018.

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See **LEADER NOTES** for answers to discussion questions.