Omega-3: Kime? Ne zaman? Nasıl?

S.B.Ü. Seyrantepe Hamidiye Etfal Eğitim ve Araştırma Hastanesi Kardiyoloji Kliniği

Doç.Dr. Ahmet Gürdal

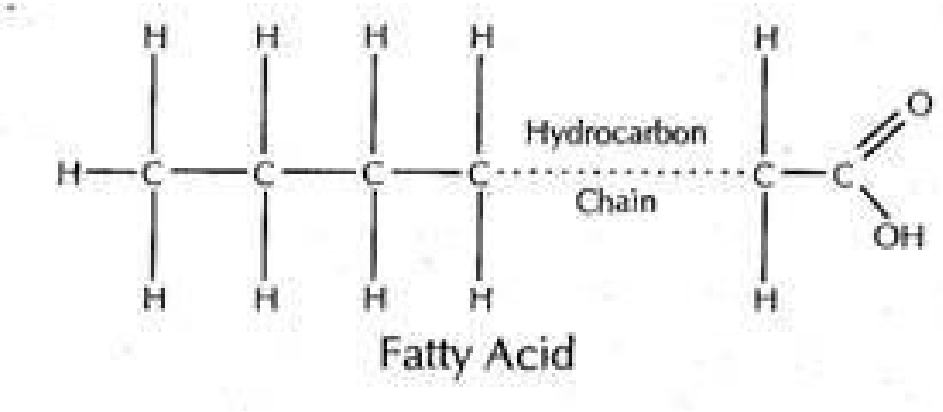
Sunum planı

- Omega-3'ü tanıyalım
- Omega-3 içeren besin kaynakları
- Geçmişten günümüze çalışmalar ve metaanalizler
- Klavuzlar ne diyor?
- Eve götürülecek mesajlar..

YAĞ ASİTLERİ

Yağ asitleri, hidrokarbon zincirli karboksilik asitlerdir. (Cn 4 – 36)

Genel Formül: CH_3-(CH_2)n-COO^-(H)



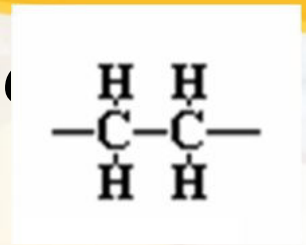
YAĞ ASİTLERİNİN ADLANDIRILMASI

Karbon sayılarına göre;

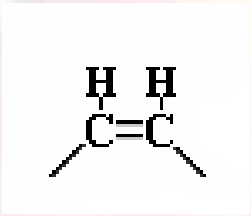
- **Kısa Zincirli Yağ Asitleri: 2-4 C atomlu**
- **Orta Zincirli Yağ Asitleri: 6 – 10 C atomlu**
- **Uzun Zincirli Yağ Asitleri: 12 – 28 C atomu**

C Atomları arasındaki bağlara göre;

I. Doymuş yağ asitl



II. Doymamış yağ asitleri

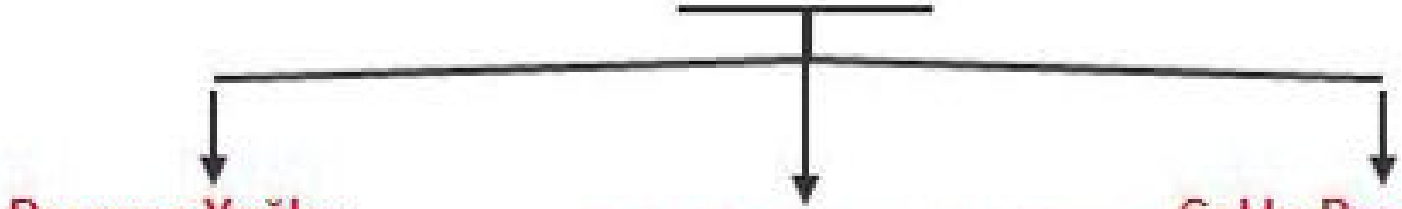


1. Tekli doymamış yağ asitleri
2. Çoklu doymamış yağ asitleri
   a. n-6 (ω-6) serisi
   b. n-3 (ω-3) serisi

Çoklu Doymamış Yağ Asitleri

- Birden fazla çift bağ içeren yağ asitleri olarak isimlendirilir. Bu yağ asitlerinin en önemlileri (C18, C20 ve C22) aşağıda sıralanmıştır
- Linoleik asit (LA); [C18:2 (n-6 omega)],
- α-linolenik asit (α-LN); [C18:3 (n-3 omega)],
- Araşidonik asit (AA); [C20:4 (n-6 omega)],
- Eikosapentaenoik asit (EPA); [C20:5 (n-3 omega)],
- Dokosahekzaenoik asit (DHA); [C22:6 (n-3 omega)] (14,15).

YAĞLAR



Doymuş Yağlar

(katı yağlar)

- Tereyağ*
- Katı margarin**
- İç yağı *
- Kuyruk yağı*
- Tam yağlı süt ve ürünleri, et ve et ürünleri*

Tekli Doymamış Yağlar

(Sıvı yağlar)

- Zeytinyağı (omega-9)
- Fındık yağı (omega-9)

Çoklu Doymamış Yağlar

(Sıvı yağlar)

- Ayçiçek yağı (omega-6)
- Mısırözü yağı (omega-6)
- Balık yağı (omega-3) EPA- DHA
- Keten tohumu, ceviz vb. (omega-3) (ALA)

Esansiyel Yağ Asitleri

- Vücudun üretemediği ve mutlaka besinler yoluyla alınması gereken bu yağ asitleri, esansiyel yağ asitleri olarak adlandırılmıştır.
- Yapılarında ÇİFT BAĞ içerirler
- Hayvanlar ve insanlar için esansiyel özelliğe sahiptirler.
- Omega 3 ve omega 6, iki önemli esansiyel yağ asidi ailesidir.
- Bu yağ asitleri oksijen transport sistemi,hücre membran fonksiyonunda önemli rol oynamaktadır. Özellikle beyin ve göz olmak üzere bir çok organ sisteminin normal büyüme ve gelişmesi için gereklidir.

OMEGA YAĞ ASİTLERİ KAYNAKLARI

	Yağ asiti	Başlıca kaynakları	Dokularda bulunuşu
n-3	α-Linolenik asit (ALA)	Kolza, keten tohumu yağı, kanola yağı, kuş üzümü yağı, yeşil yapraklar	Az miktarda
	EPA (Eicosapentoenoik)	Su ürünleri, anne sütü	Az miktarda
	DHA (Docosahexsaenoik)	Su ürünleri, anne sütü	Beyin ve retinada fosfolipitlerin bileşeni
n-6	Linoleik asit	Bitkisel yağlar (mısır, yer fıstığı, pamuk, soya yağı) ve bitkiler	Diğerlerinden biraz daha fazla
	Araşidonik asit	Karaciğer, beyin, et, yer fıstığı yağı	Hücre zarı lipitlerinin bileşeni
n-9	Oleik asit	Zeytinyağı, fındık yağı	Beynin beyaz maddesinde, miyelinde
	Eicosantrienoik asit	Hayvan ve bitki dokusunda çok az	Elzem yağ asiti yetersizliğinde artar
	Miristoleik asit	Süt ve balıkta az	Az miktarda
	Palmitoleik asit	Süt ve balıkta az	Az miktarda

OMEGA-3 KAYNAKLARI

BİTKİSEL KAYNAKLAR

- Keten Tohumu Yağı
- Kanola Yağı
- Soya Fasulyesi
- Ceviz
- Balkabağı Çekirdeği
- Kenevir Tohumu Yağı Semizotu
- Kuru Baklagiller
- Kolza Tohumu

Bitkisel OMEGA-3 Kullanımı

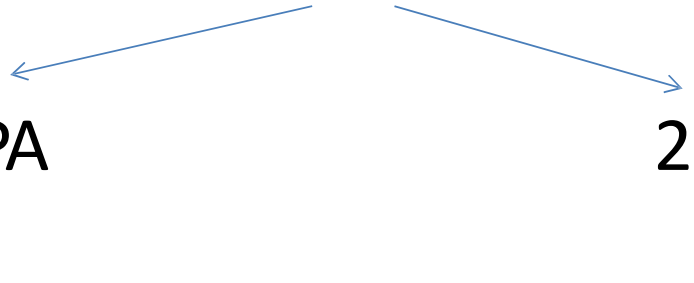
- ✓ Bitkisel omega-3'lerden bedenimiz direkt olarak yararlanamıyor. Alfa linolenik asidin bedenimizde EPA ve DHA'ya dönüşmesi gerekiyor.

- ✓ Dönüşüm oranı ise çok düşük, EPA'da yüzde 5-7'yi, DHA'da yüzde 1-3'ü geçmiyor.

- ✓ Dolayısıyla hayvansal omegalara, yani balık, krill, havyar yağı omegalarına öncelik vermek daha doğrudur.

Bitki kaynaklı n-3 yağ asitleri:

α-linolenik asit (LNA) (18:3)



20:5 EPA

22:6 DHA

Prostoglandin E3 (PGE3)

Tromboksan A3 (TXA3)

Biochemical Pharmacology 2009;77(6):937-946.
Brown A. Understanding Food. Fish and Shellfish.Wadsworth /Thomson Learning, USA, 2000;299.

HAYVANSAL KAYNAKLAR

- Özellikle soğuk su balıkları ve yağlı balıklar, kabuklu deniz ürünleri ve az miktarda yumurtadır.

- Kültür balıklarında n-3 yağ asitleri daha az bulunur.

- Ayrıca anne sütünde de önemli miktarda bulunmaktadır.

- Balıkların n-3 içerikleri de farklıdır. En çok n-3 içeren balıklar soğuk su ya da derin dip balıklarıdır.

- Uskumru, ringa, tuna, somon, sardalye gibi soğuk su balıkları yağlı olup, n-3'ten zengindir.

- Balıkların n-3 yağ asit kaynakları algler ve planktonlardandır.

1 g balık yağı (EPA+DHA gereksinimi karşılamak) için tüketilmesi gereken balık miktarı

	Miktar (g/gün)
Taze ton balığı	70-360
Sardalya	60-90
Somon	60-135
Orkinos	60-250
Ringa Balığı	45-60
Alabalık	90-105
Pisi (Tarança) Balığı	90-225
Mezgit Balığı	450
Yayın Balığı	450
Dil balığı	210
İstiridye (pasifik/ doğuya özgü/çiftlik)	75/195/240
İstakoz	225-1275
Yengeç	255
Karides	330
İstiridye	375

Process Biochemistry 2005;40:3627–3652

EİKOSAPENTAENOİK ASİT (EPA) VE DOKOSAHEKZAENOİK ASİT(DHA)

- n -3 omega yağ asitlerinin vücutta ki en önemli aktif formlarıdır.

- Bu yağ asitleri genel olarak deniz algleri tarafından sentezlenir, plankton ve diğer küçük deniz hayvanları tarafından tüketilerek besin zincirine katılmış olurlar.

- Beyin ve retina membranının en önemli bileşiği olan DHA, ALA(alfa linoneik asit)eksikliğinde yeterli miktarda oluşamaz. **Diyetle çok yüksek miktarda alınan omega 6 ,** EPA ve DHA'nın sentezini inhibe eder.

- Bu nedenle linoleik asit (LA) içeren mısır ve ayçiçek yağınca zengin ve alfa linoneik asitce (ALA) düşük diyetler EPA ve DHA eksikliğine sebep olur.

OMEGA 6 ve OMEGA 3 YAĞ ASİTLERİNİN DENGESİ

- Dünya Sağlık Örgütü; günlük yağ asidi %2,5-9 omega-6 ve % 0.5-2 omega-3 yağ asidi alımı önermektedir.(yaklaşık oran 5:1 olmalı)

- Ancak; günümüz beslenme alışkanlıklarına bakıldığında bu oranın 25:1 ve üzeri olduğu tespit edilmiştir.

OMEGA 3 VE OMEGA 6 YAĞ ASİTLERİNİ ÖNERİLEN ORANDA NASIL ALABİLİRİM?;

- Haftada en az 2-3 kez balık yenmelidir.
- Omega-6 yağ asidini içeren tohum yağı ve bitkisel yağlardan (ve bunları içeren işlenmiş yiyeceklerden) kaçınılmalıdır.
- Hamileler ve süt veren anneler haftada 4-5 gün balık yemelidir.
- Gerekirse, omega 3 açığı balık yağı gibi bir omega-3 kaynağı ile desteklenmelidir.
- Her gün omega 3 kaynağı olarak 2-3 adet ceviz yenmelidir. Balık kadar olmasa da değerli bir Omega 3 kaynağı olan ceviz kalbi koruyup ve beyin performansını artırmaktadır.
- Omega 3 kaynağı olan tohum ve kuru yemişlerin taze ve kabuklu tüketilmesine özen gösterilmelidir.
- Ticari amaçla soya ve mısır ile beslenen küçük baş hayvanların etlerinde omega 6 artığı, bunula birlikte merada ya da kaba yemle beslenen küçük baş hayvanların etlerinde ki omega 3 oranının artığı belirtilmiştir.
- Bu yüzden mümkün oldukça merada ya da kaba yemle beslenen hayvanların etlerini tüketmeye özen gösterilmelidir.

OMEGA-3'ÜN KARDİYOVASKÜLER SİSTEM ÜZERİNE OLAN BAŞLICA ETKİLERİ

- Antiaritmik
- Antitrombotik
- Antiaterosklerotik
- Anti-inflamatuar
- Endotel fonksiyonunu düzenleme
- Hafif düzeyde hipotansif etkili
- Trigliserid düzeylerini düşürme
- Aterosklerotik plak oluşumunu geciktirme

Process Biochemistry 2005;40:3627–3652

YAPILAN İLK ÇALIŞMALAR..

- 1970’li yıllarda daha çok hayvansal yağla (deniz ürünleri)beslendikleri halde; **Grönland Eskimolarında** koroner kalp hastalıkları, kanser ve romatoit artrit’in diğer toplumlara göre daha az görüldüğü görülmüş.

- 1980'lerde balıktaki n-3 yağ asitlerinin kolesterol düzeyleri üzerine olumlu etkisi olduğu gösterilmiş..

Chang JPC, et al. Cardiovascular Psychiatry and Neurology 2009.
Poultry Science 2000; 79:961–970

YAPILAN İLK ÇALIŞMALAR..

Bir çalışmada, erkeklere verilen balık yağı takviyelerinin nitrik oksit üretimini %43 arttırdığı; böylece endotel disfonksiyondan koruduğu gösterilmiştir.

Amer J of Clin Nutr 1997;65:459-64.

Başka bir çalışmada, EPA ve DHA'nın hiperkolesterolemiyi ve trombosit fonksiyonlarını düzelttiği;

Biosci Biotechnol Biochem 1999;63: 111-9.

Diğer bir çalışmada da, kolesterol düzeylerini düşürmekle beraber lenfosit fonksiyonlarını baskılayarak aterosklerotik süreci yavaşlattığı gösterilmiş.

Lipids 1996;31:737-45.

- Yaşam tarzı değişikliğine ek olarak, 20 hafta süre ile 3 g balık yağı (360 mg DHA, 540 mg EPA) tüketen yetişkin bireylerin;

- Bel çevresinde (%1,3), trigliserid düzeylerinde (%27,3), sistolik ve diastolik kan basıncında (%33,3) ve metabolik sendrom görülme sıklığında (%29) azalma olduğu belirlenmiştir.

Journal of Functional Foods 2015;19:922-928.

November 2012

Omega 3 Fatty Acids and Cardiovascular Outcomes

Systematic Review and Meta-Analysis

Sradha Kotwal, BHB, MBChB, FRACP; Min Jun, BSc (Hons), MSc; David Sullivan, MBBS, FRACP, FRCPA; Vlado Perkovic, MBBS, PhD, FRACP; Bruce Neal, MBChB, PhD, FRACP

Background—Early trials evaluating the effect of omega 3 fatty acids (ω-3 FA) reported benefits for mortality and cardiovascular events but recent larger studies trials have variable findings. We assessed the effects of ω-3 FA on cardiovascular and other important clinical outcomes.

Methods and Results—We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials for all randomized studies using dietary supplements, dietary interventions, or both. The primary outcome was a composite of cardiovascular events (mostly myocardial infarction, stroke, and cardiovascular death). Secondary outcomes were arrhythmia, cerebrovascular events, hemorrhagic stroke, ischemic stroke, coronary revascularization, heart failure, total mortality, nonvascular mortality, and end-stage kidney disease. Twenty studies including 63 030 participants were included. There was no overall effect of ω-3 FA on composite cardiovascular events (relative risk [RR]=0.96; 95% confidence interval [CI], 0.90–1.03; *P*=0.24) or on total mortality (RR=0.95; 95% CI, 0.86–1.04; *P*=0.28). ω-3 FA did protect against vascular death (RR=0.86; 95% CI, 0.75–0.99; *P*=0.03) but not coronary events (RR=0.86; 95% CI, 0.67–1.11; *P*=0.24). There was no effect on arrhythmia (RR=0.99; 95% CI, 0.85–1.16; *P*=0.92) or cerebrovascular events (RR=1.03; 95% CI, 0.92–1.16; *P*=0.59). Adverse events were more common in the treatment group than the placebo group (RR=1.18, 95% CI, 1.02–1.37; *P*=0.03), predominantly because of an excess of gastrointestinal side effects.

Conclusions—ω-3 FA may protect against vascular disease, but the evidence is not clear-cut, and any benefits are almost certainly not as great as previously believed. (***Circ Cardiovasc Qual Outcomes*. 2012;5:808-818.**)

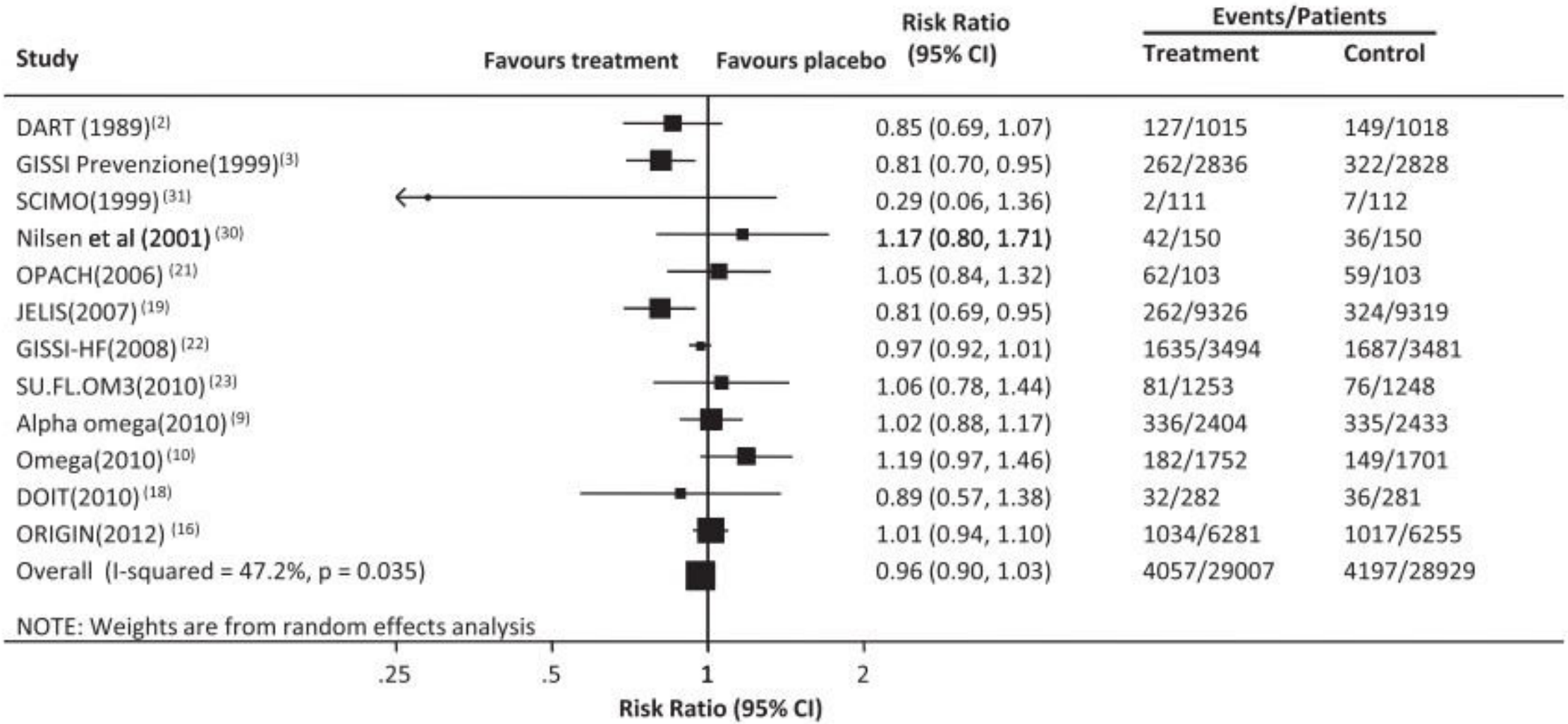


Figure 2. Effect of ω-3 fatty acids on composite cardiovascular outcomes. CI indicates confidence interval.

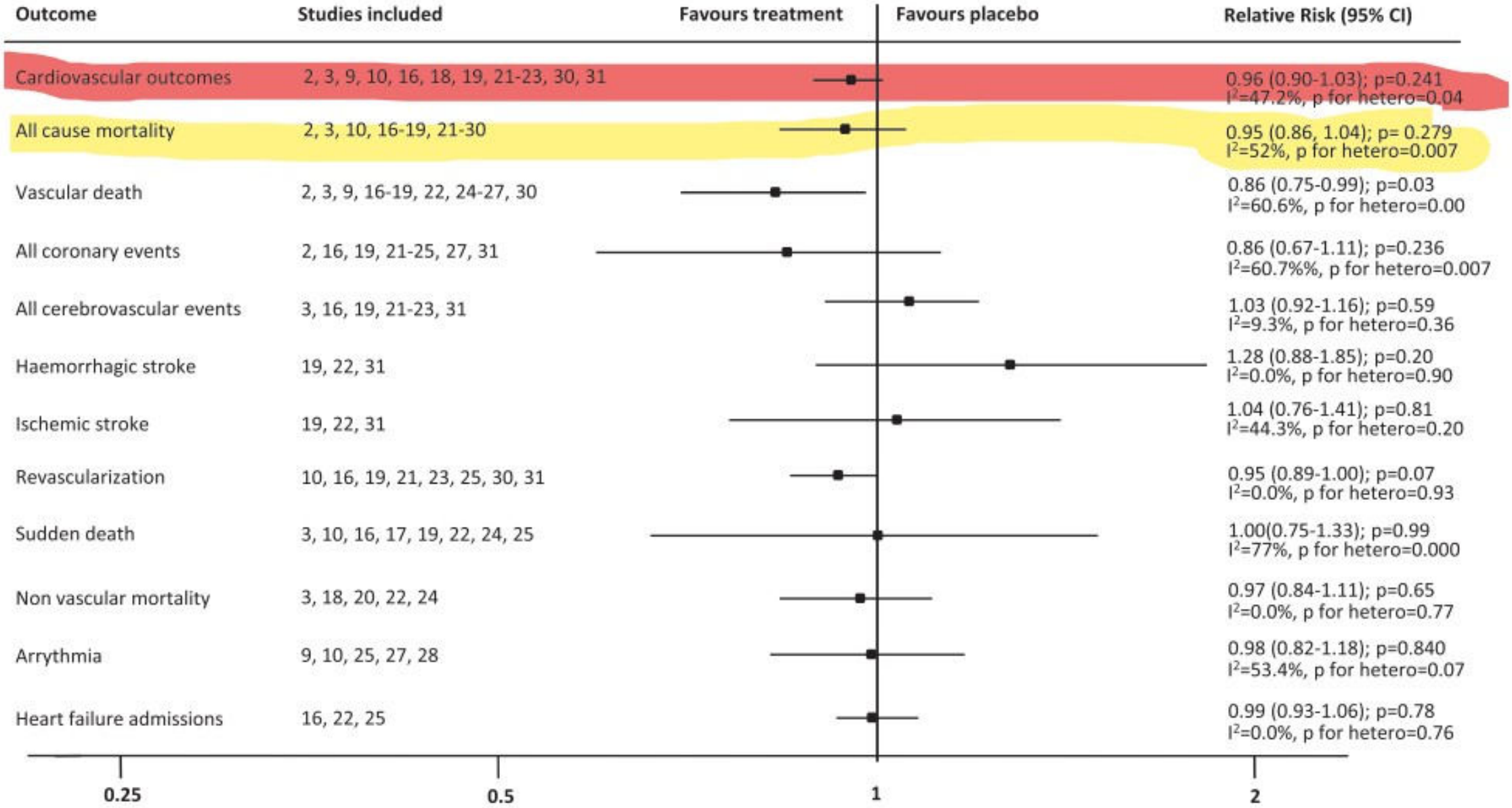


Figure 3. Effect of ω-3 fatty acids on all outcomes. CI indicates confidence interval.

Research

JAMA Cardiology | Original Investigation

Associations of Omega-3 Fatty Acid Supplement Use With Cardiovascular Disease Risks

Meta-analysis of 10 Trials Involving 77 917 Individuals

Theingi Aung, MBBS, FRCP; Jim Halsey, BSc; Daan Kromhout, PhD; Hertzel C. Gerstein, MD; Roberto Marchioli, MD; Luigi Tavazzi, MD; Johanna M. Geleijnse, PhD; Bernhard Rauch, MD; Andrew Ness, PhD, FFPH; Pilar Galan, MD, PhD; Emily Y. Chew, MD; Jackie Bosch, PhD; Rory Collins, FMedSci, FRCP; Sarah Lewington, DPhil; Jane Armitage, FRCP, FFPH; Robert Clarke, MD, FRCP, FFPH; for the Omega-3 Treatment Trialists' Collaboration

IMPORTANCE Current guidelines advocate the use of marine-derived omega-3 fatty acids supplements for the prevention of coronary heart disease and major vascular events in people with prior coronary heart disease, but large trials of omega-3 fatty acids have produced conflicting results.

OBJECTIVE To conduct a meta-analysis of all large trials assessing the associations of omega-3 fatty acid supplements with the risk of fatal and nonfatal coronary heart disease and major vascular events in the full study population and prespecified subgroups.

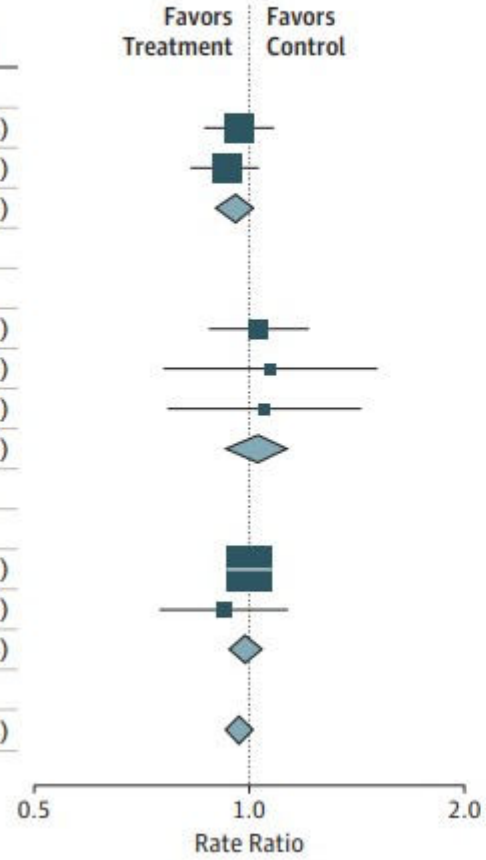
Supplemental content

Table. Characteristics of Included Trials

Study (Year)	Patients, No.	Dose of EPA/DHA (mg/d)	Male, No. (%)	Mean Trial Duration, y	Mean (SD) Age, y	No. (%)			
						Prior CHD	Prior Stroke	Prior Diabetes	Statin Use
DOIT (2010)	563	1150/800	563 (100)	3	70 (3)	133 (23.6)	37 (6.6)	46 (8.2)	NA
AREDS-2 (2014)	4203	650/350	1816 (43.2)	4.5	74 (NA)	405 (9.7)	211 (5.0)	546 (13.0)	1866 (44.4)
SU.FOL.OM3 (2010)	2501	400/200	1987 (79.4)	4.7	61 (NA)	1863 (74.5)	638 (25.5)	440 (17.9)	2079 (83.1)
JELIS (2007)[a,b]	18 645	1800/NA	5859 (31.4)	4.6	61 (8)	NA	NA	3040 (16.3)	18 645 (100.0)
Alpha Omega (2010)	4837	226/150	3783 (78.2)	3.3	69 (6)	4837 (100.0)	345 (7.2)	1014 (21.0)	4122 (85.2)
OMEGA (2010)	3818	460/380	2841 (74.4)	1	64 (NA)	796 (22.5)	192 (5.5)	948 (27.0)	3566 (94.2)
R&P (2013)	12 505	500/500	7687 (61.5)	5	64 (NA)	Not stated (30)	594 (4.8)	7494 (59.9)	12 505 (100.0)
GISSI-HF (2008)	6975	850/950	5459 (78.3)	3.9	67 (11)	3614 (51.8)	346 (5.0)	1974 (28.3)	NA
ORIGIN (2012)	12 536	465/375	8150 (65.0)	6.2	64 (8)	8094 (64.6)	10 877 (86.8)	11 081 (88.4)	6739 (53.8)
GISSI-P[b] (1999)	11 334	850/1700	9658 (85.2)	3.5	59 (11)	11 334 (100.0)	NA	2139 (18.9)	NA
Total	77 917	NA	47 803 (61.4)	4.4	64	31 076/46 767 (66.4)	13 240/47 938 (27.6)	28 722 (36.9)	49 522 (83.4)

Figure 1. Associations of Omega-3 Fatty Acids With Major Vascular Events

Source	No. of Events (%) Treatment	Control	Rate Ratios (CI)
Coronary heart disease			
Nonfatal myocardial infarction	1121 (2.9)	1155 (3.0)	0.97 (0.87-1.08)
Coronary heart disease death	1301 (3.3)	1394 (3.6)	0.93 (0.83-1.03)
Any	3085 (7.9)	3188 (8.2)	0.96 (0.90-1.01)
			P=.12
Stroke			
Ischemic	574 (1.9)	554 (1.8)	1.03 (0.88-1.21)
Hemorrhagic	117 (0.4)	109 (0.4)	1.07 (0.76-1.51)
Unclassified/other	142 (0.4)	135 (0.3)	1.05 (0.77-1.43)
Any	870 (2.2)	843 (2.2)	1.03 (0.93-1.13)
			P=.60
Revascularization			
Coronary	3040 (9.3)	3044 (9.3)	1.00 (0.93-1.07)
Noncoronary	305 (2.7)	330 (2.9)	0.92 (0.75-1.13)
Any	3290 (10.0)	3313 (10.2)	0.99 (0.94-1.04)
			P=.60
Any major vascular event	5930 (15.2)	6071 (15.6)	0.97 (0.93-1.01)
			P=.10



The number of events by allocated treatment are presented for individual trials and subgroups of trials; participants can contribute only once to subtotals and totals of major vascular events. Rate ratios for individual trials or subgroups of trials are indicated by squares and 99% CIs by horizontal lines. Overall totals and their 95% confidence intervals are represented by diamonds. The size of the squares and the diamonds are proportional to the statistical information conveyed.

statin use.

CONCLUSIONS AND RELEVANCE This meta-analysis demonstrated that omega-3 fatty acids had no significant association with fatal or nonfatal coronary heart disease or any major vascular events. It provides no support for current recommendations for the use of such supplements in people with a history of coronary heart disease.

EVAPORATE STUDY DESIGN

Received: 15 September 2017 | Revised: 17 November 2017 | Accepted: 21 November 2017

DOI: 10.1002/clc.22856

WILEY CLINICAL CARDIOLOGY

TRIAL DESIGNS

Effect of Vascepa (icosapent ethyl) on progression of coronary atherosclerosis in patients with elevated triglycerides (200–499 mg/dL) on statin therapy: Rationale and design of the EVAPORATE study

Matthew Budoff[1] | J. Brent Muhlestein[2,3] | Viet T. Le[2] | Heidi T. May[2] | Sion Roy[1] | John R. Nelson[4]

EVAPORATE: Effect of EPA on Improving Coronary Atherosclerosis in People With High Triglycerides Taking Statin Therapy

Randomized, Double-Blind, Placebo-Controlled Trial

Patient Population (N=~80)

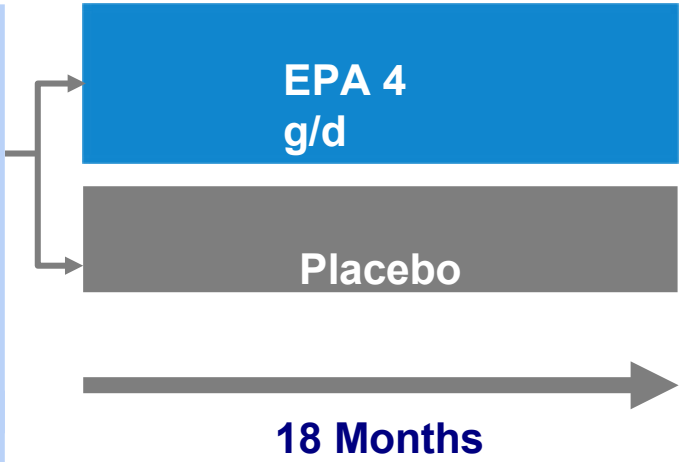
- 30–85 years of age
- TG: 135–499 mg/dL
- LDL-C >40 mg/dL and ≤115 mg/dL (on statin)
- ≥1 angiographic stenosis with ≥20% narrowing by CTA
- No history of MI, stroke, or life-threatening arrhythmia within the prior 6 months and no history of CABG

Primary endpoint

- Progression rates of low attenuation plaque

Secondary endpoints include

- Plaque morphology and composition
- Markers of inflammation (Lp-PLA_2)
- LDL-C and HDL-C



Estimated Study Completion Date: September 2019

The EVAPORATE study seeks to determine whether IPE 4g/d will result in a greater change from baseline in plaque volume measured by serial multidetector computed tomography (MDCT) than placebo in statin-treated patients

CABG=coronary artery bypass graft; CTA=computed tomography angiography.

EVAPORATE Clinical Trial. https://clinicaltrials.gov/ct2/show/NCT02926027. Updated February 08, 2018. Accessed June 19, 2018.

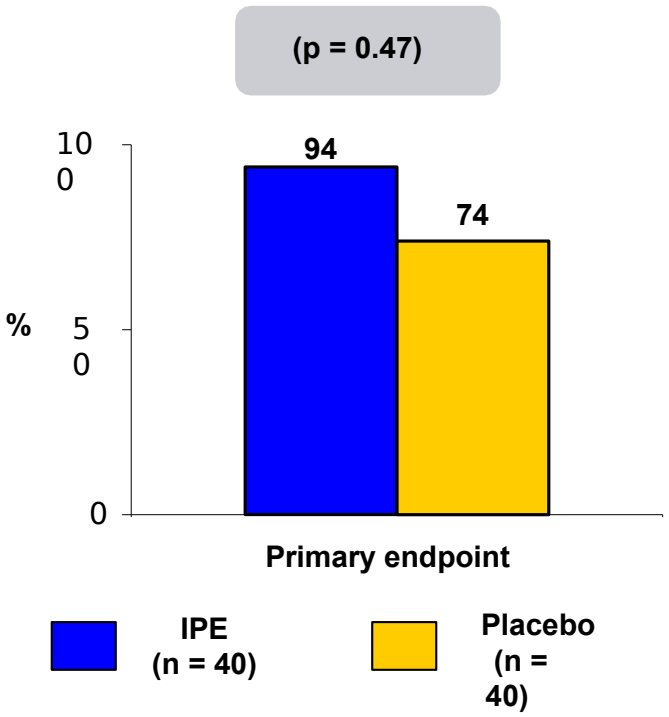
TABLE 2 EVAPORATE study endpoints

Primary endpoint
Change in low-attenuation plaque volume as measured by MDCTA and defined as −50 to 50 HU
Secondary endpoints
Incident plaque rates; quantitative changes in different plaque types and morphology
Changes in markers of inflammation including Lp-PLA_2 and hsCRP
Changes in lipids and lipoproteins including standard lipid panel, lipoproteins, remnants, Apo-A1/remnant ratio, EPA, AA, and EPA/AA ratio
Relationship between changes in the above with noncalcified coronary plaque burden and/or plaque-vulnerability features

Abbreviations: AA, arachidonic acid; Apo-A1, apolipoprotein A1; EPA, eicosapentaenoic acid; EVAPORATE, Effect of Vascepa on Improving Coronary Atherosclerosis in People With High Triglycerides Taking Statin Therapy study; hsCRP, high-sensitivity C-reactive protein; HU, Hounsfield

EVAPORATE

Trial Description: Patients with known angiographic disease on statins were randomized to either icosapent ethyl (IPE) 4 g/day or placebo. Interim results at 9 months were presented.



RESULTS

- Primary endpoint, % change in low attenuation plaque volume, for IPE vs. placebo: 94% vs. 74% (p = 0.47)
- Change in fibrofatty plaque volume: 25% vs. 87% (p = 0.65); change in total plaque volume: 26% vs. 15% (p = 0.0004)

CONCLUSIONS

- Interim results at 9 months indicate that IPE 4 g/day does not reduce low attenuation plaque volume compared with placebo, but does reduce total plaque volume
- These are interim results; planned duration of follow-up is 18 months
- These results may help explain the CV benefit noted with IPE in the REDUCE-IT trial

Presented by Dr. Matthew J. Budoff at AHA 2019

ORIGINAL ARTICLE

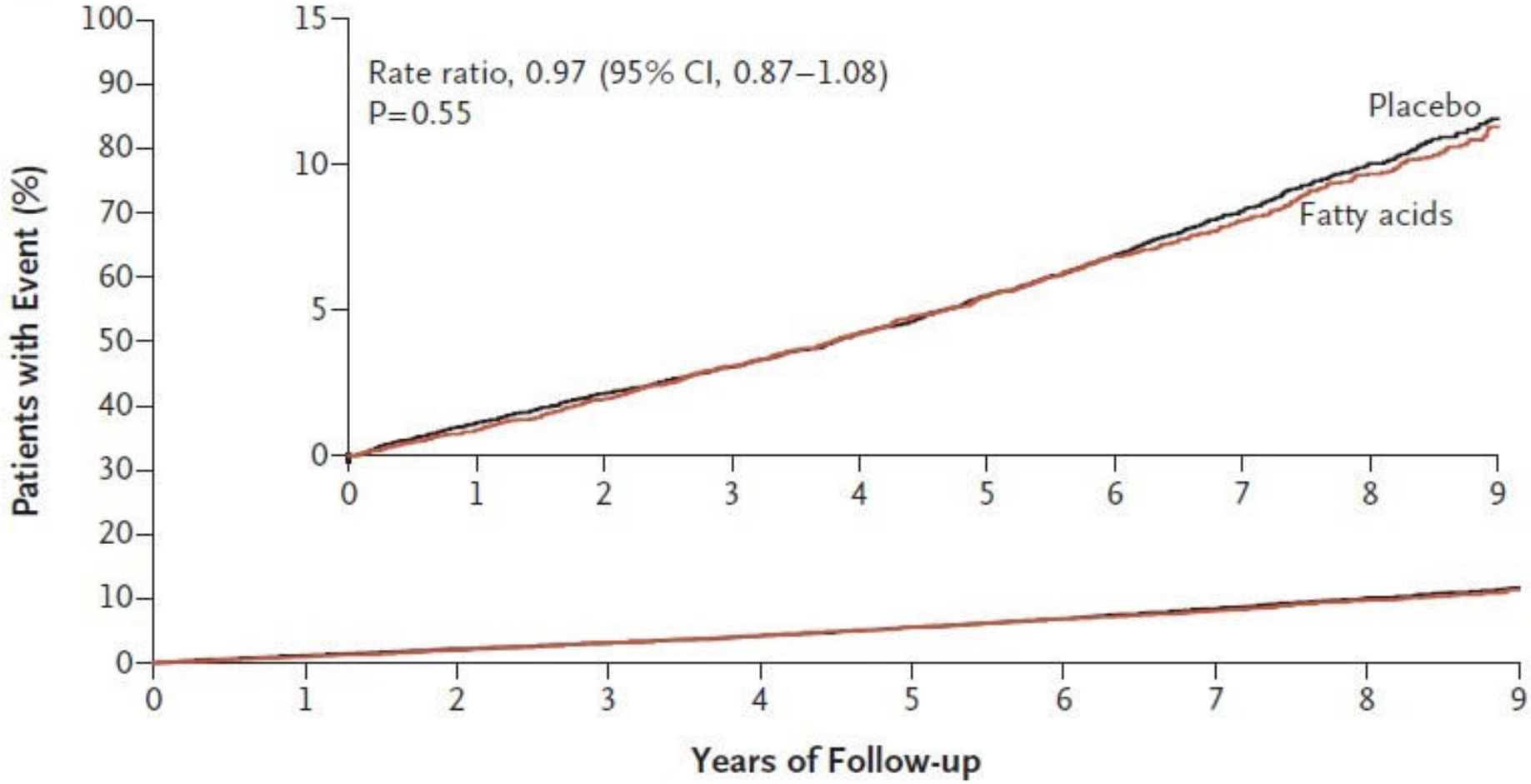
Effects of n–3 Fatty Acid Supplements in Diabetes Mellitus

The ASCEND Study Collaborative Group*

This article was published on August 26, 2018, at NEJM.org.

DOI: 10.1056/NEJMoa1804989

A First Serious Vascular Event



No. at Risk										
Placebo	7740	7627	7503	7377	7222	7047	5792	3934	2224	1428
Fatty acids	7740	7646	7519	7369	7218	7050	5804	3922	2198	1430
Cumulative benefit per 1000 patients in fatty acid group		3±2	2±2	0±3	0±3	0±4	1±4	3±5	4±6	3±7

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 3, 2019 VOL. 380 NO. 1

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

Deepak L. Bhatt, M.D., M.P.H., P. Gabriel Steg, M.D., Michael Miller, M.D., Eliot A. Brinton, M.D., Terry A. Jacobson, M.D., Steven B. Ketchum, Ph.D., Ralph T. Doyle, Jr., B.A., Rebecca A. Juliano, Ph.D., Lixia Jiao, Ph.D., Craig Granowitz, M.D., Ph.D., Jean-Claude Tardif, M.D., and Christie M. Ballantyne, M.D., for the REDUCE-IT Investigators*

ABSTRACT

BACKGROUND

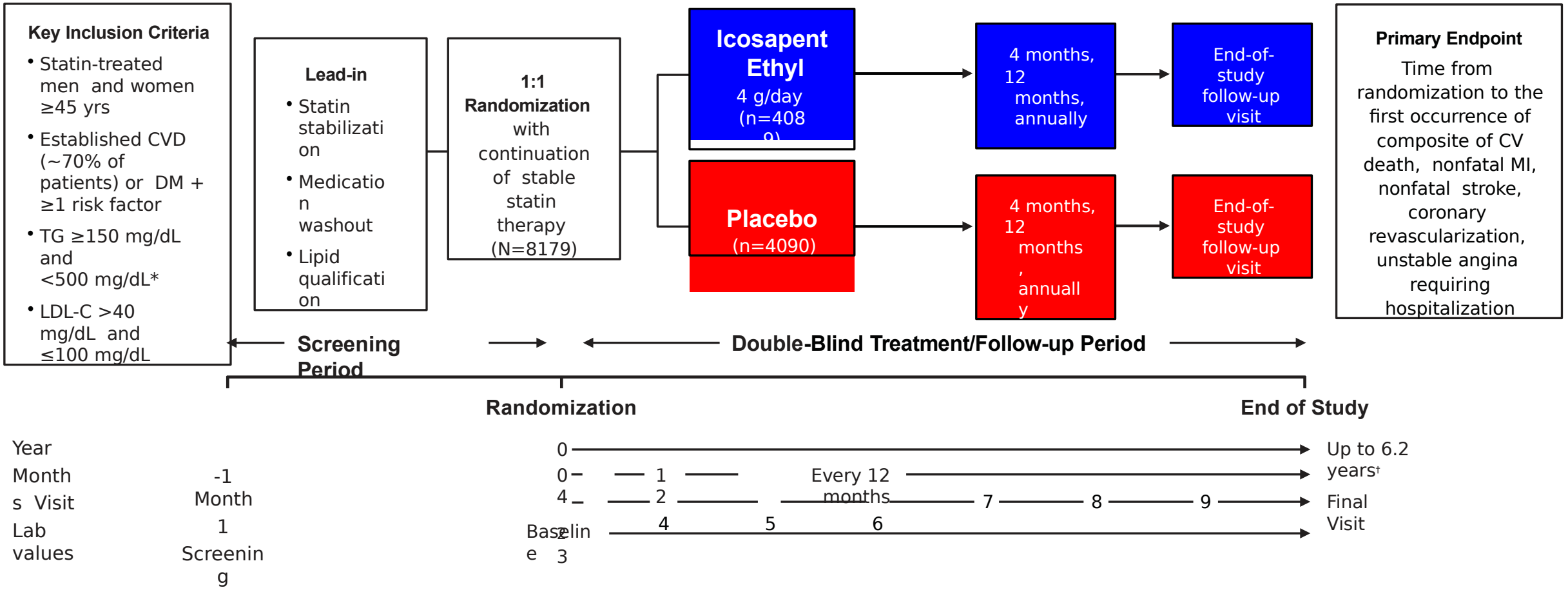
Patients with elevated triglyceride levels are at increased risk for ischemic events. Icosapent ethyl, a highly purified eicosapentaenoic acid ethyl ester, lowers triglyceride levels, but data are needed to determine its effects on ischemic events.

METHODS

We performed a multicenter, randomized, double-blind, placebo-controlled trial involving patients with established cardiovascular disease or with diabetes and other risk factors, who had been receiving statin therapy and who had a fasting triglyceride level of 135 to 499 mg per deciliter (1.52 to 5.63 mmol per liter) and a low-density lipoprotein cholesterol level of 41 to 100 mg per deciliter (1.06 to 2.59 mmol per liter). The patients were randomly assigned to receive 2 g of icosapent ethyl twice daily (total daily dose, 4 g) or placebo. The primary

From Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston (D.L.B.); FACT (French Alliance for Cardiovascular Trials), Département Hospitalo-Universitaire FIRE (Fibrose, Inflammation, and Remodeling), Assistance Publique–Hôpitaux de Paris, Hôpital Bichat, Université Paris-Diderot, INSERM Unité 1148, Paris (P.G.S.); National Heart and Lung Institute, Imperial College, Royal Brompton Hospital, London (P.G.S.); the Department of Medicine, University of Maryland School of

REDUCE-IT Design



*Due to the variability of triglycerides, a 10% allowance existed in the initial protocol, which permitted patients to be enrolled with qualifying triglycerides ≥135 mg/dL. Protocol amendment 1 (May 2013) changed the lower limit of acceptable triglycerides from 150 mg/dL to 200 mg/dL, with no variability allowance.

† Median trial follow-up duration was 4.9 years (minimum 0.0, maximum 6.2 years).

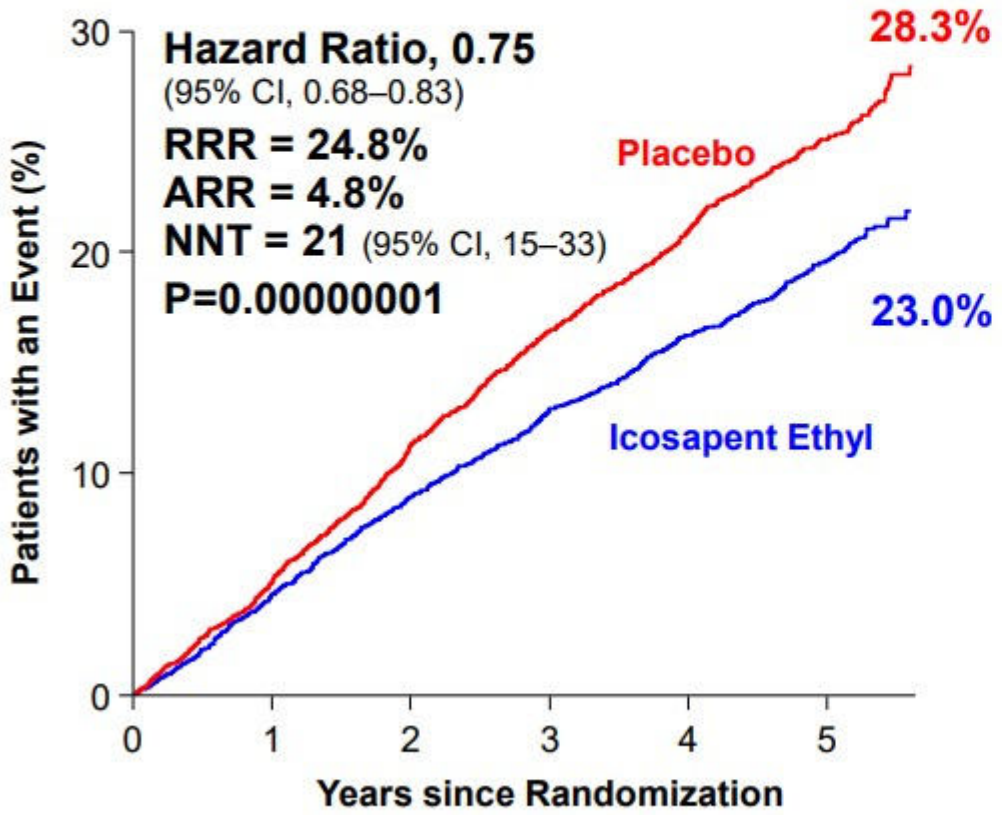
Bhatt DL, Steg PG, Brinton EA, et al; on behalf of the REDUCE-IT Investigators. Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clin Cardiol.* 2017;40:138-148. ClinicalTrials.gov number, NCT01492361.

Primary and Key Secondary Composite Endpoints

reduce-it

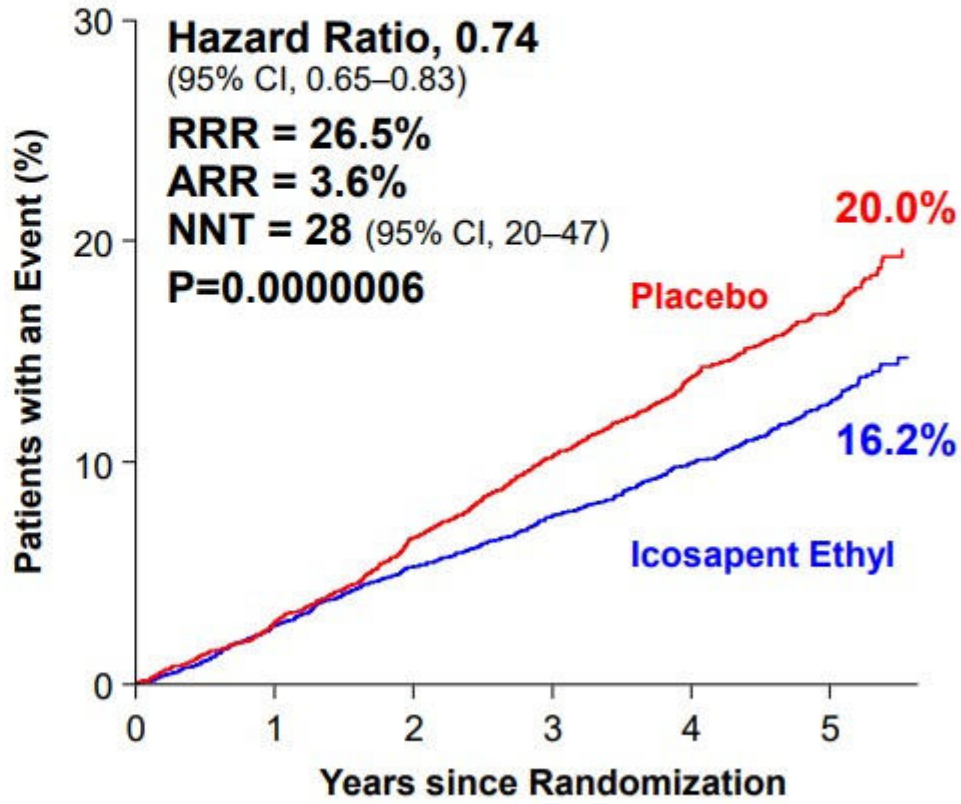
Primary Composite Endpoint:

CV Death, MI, Stroke, Coronary Revasc, Unstable Angina



Key Secondary Composite Endpoint:

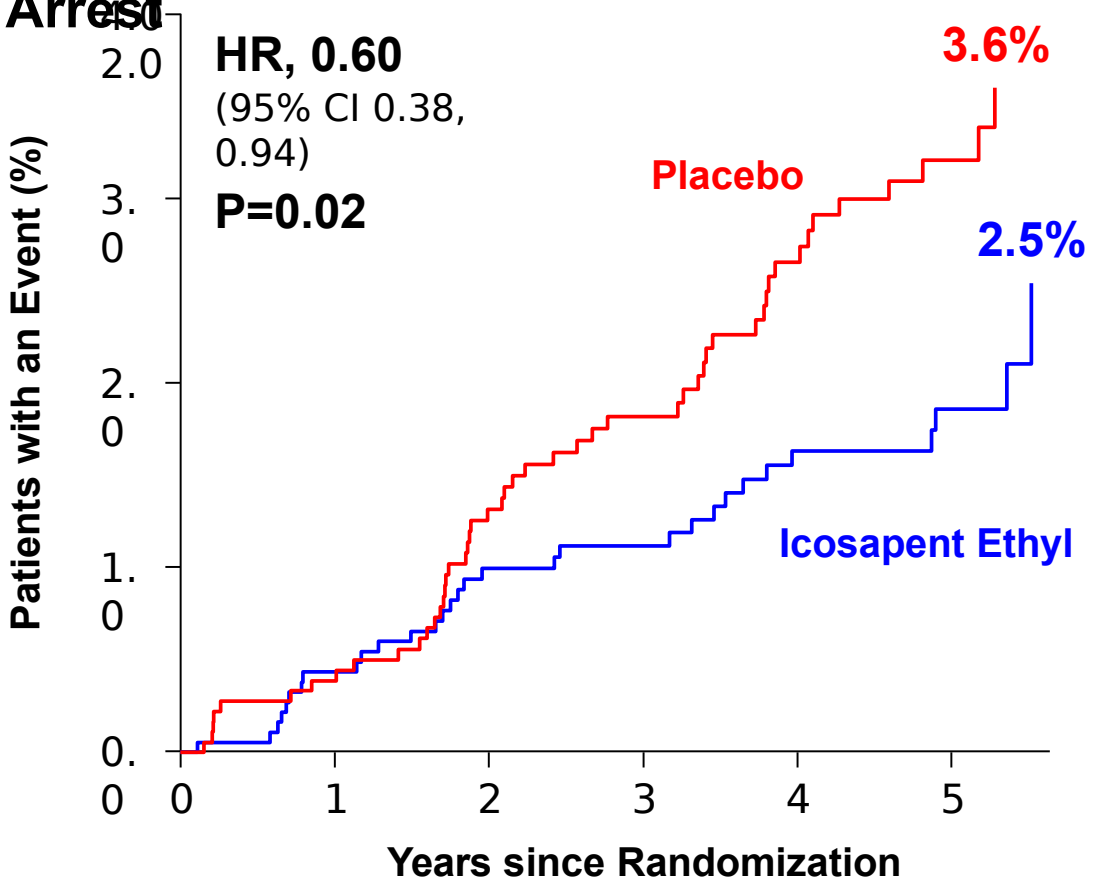
CV Death, MI, Stroke



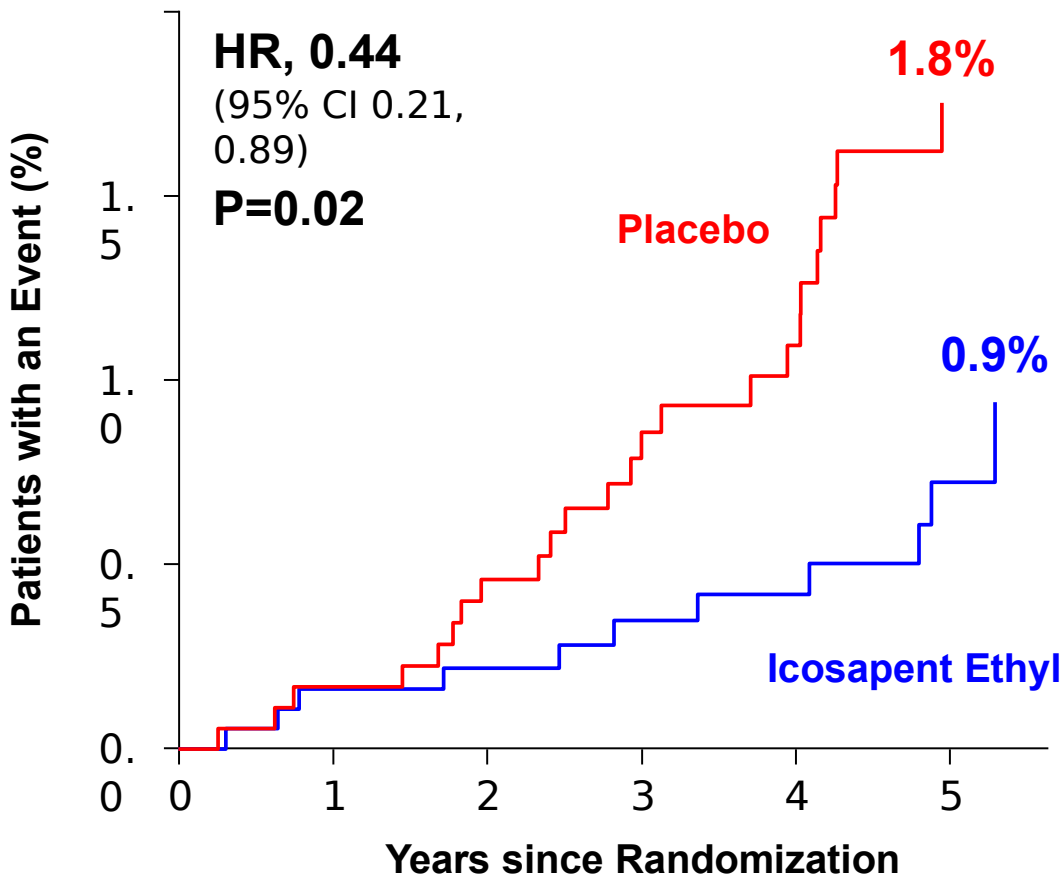
Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med.* 2019; 380:11-22. Bhatt DL. AHA 2018, Chicago.

Cardiac Arrest and Sudden Cardiac Death in Patients with Prior MI

Sudden Cardiac Death



Cardiac



Results consistently statistically significant by ~ 4 years

Bhatt DL, Steg PG, Miller M, et al., ESC 2021 (virtual)

Safety

Safety was generally consistent with the full study.

No differences were observed between icosapent ethyl and placebo in overall tolerability or adverse events in patients with prior MI.

More bleeding occurred with icosapent ethyl vs. placebo in patients with prior MI.

More atrial fibrillation/flutter occurred with icosapent ethyl vs. placebo.

End Point	Icosapent Ethyl (N=4089)	Placebo (N=4090)	Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)			
Primary composite	705 (17.2)	901 (22.0)	0.75 (0.68–0.83)	<0.001
Key secondary composite	459 (11.2)	606 (14.8)	0.74 (0.65–0.83)	<0.001
Cardiovascular death or nonfatal myocardial infarction	392 (9.6)	507 (12.4)	0.75 (0.66–0.86)	<0.001
Fatal or nonfatal myocardial infarction	250 (6.1)	355 (8.7)	0.69 (0.58–0.81)	<0.001
Urgent or emergency revascularization	216 (5.3)	321 (7.8)	0.65 (0.55–0.78)	<0.001
Cardiovascular death	174 (4.3)	213 (5.2)	0.80 (0.66–0.98)	0.03
Hospitalization for unstable angina	108 (2.6)	157 (3.8)	0.68 (0.53–0.87)	0.002
Fatal or nonfatal stroke	98 (2.4)	134 (3.3)	0.72 (0.55–0.93)	0.01
Death from any cause, nonfatal myocardial infarction, or nonfatal stroke	549 (13.4)	690 (16.9)	0.77 (0.69–0.86)	<0.001
Death from any cause	274 (6.7)	310 (7.6)	0.87 (0.74–1.02)	—

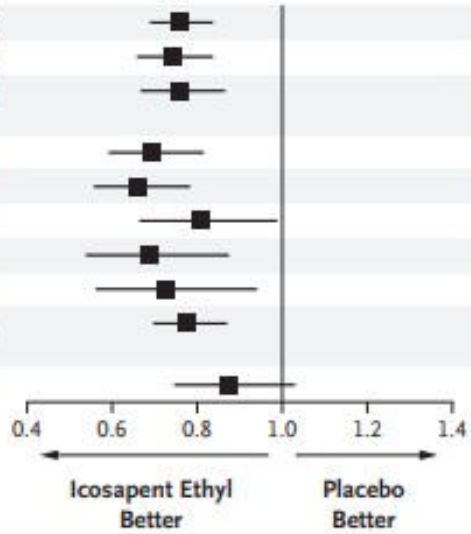


Figure 4. Hierarchical Testing of End Points.

Shown is the prespecified plan for hierarchical testing of end points. The rates of all end points up to death from any cause were significantly lower in the icosapent ethyl group than in the placebo group.

CONCLUSIONS

Among patients with elevated triglyceride levels despite the use of statins, the risk of ischemic events, including cardiovascular death, was significantly lower among those who received 2 g of icosapent ethyl twice daily than among those who received placebo. (Funded by Amarin Pharma; REDUCE-IT ClinicalTrials.gov number, NCT01492361.)

REDUCE-IT çalışmasındaki soru işaretleri??

- Daha önce yapılan onlarca çalışma negatif sonlamışken, bu çalışma neden anlamlı çıktı? (önceki çalışmaların dizaynı?, ilaçların yapısı? (bu çalışmada saf EPA, diğer çalışmalarda genellikle EPA+DHA)

- Plasebo olarak kullanılan *mineral oil in* kontrol hastalarında LDL, apoB ve CRP'yi yükselttiği görüldü('tested a good drug or a bad placebo').

- EPA ile nötr bir plasebo karşılaştırılsa nasıl bir sonuç çıkar?

- Trigliserid düzeylerinden bağımsız faydalı (Başka bir mekanizma mı?)

Recent Clinical Trials Shed New Light on the Cardiovascular Benefits of Omega-3 Fatty Acids

Penny M. Kris-Etherton, PhD, RDN[a]; *Chesney K. Richter*, PhD[b]; *Kate J. Bowen*, PhD[a]; *Ann C. Skulas-Ray*, PhD[b]; *Kristina Harris Jackson*, PhD, RDN[c]; *Kristina S. Petersen*, PhD[a]; *William S. Harris*, PhD[c,d]

[a]PENNSYLVANIA STATE UNIVERSITY, UNIVERSITY PARK, PENNSYLVANIA; [b]UNIVERSITY OF ARIZONA, TUCSON, ARIZONA; [c]OMEGA QUANT ANALYTICS, LLC, SIOUX FALLS, SOUTH DAKOTA; [d]UNIVERSITY OF SOUTH DAKOTA, SIOUX FALLS, SOUTH DAKOTA

ABSTRACT: Three recent clinical trials have demonstrated the benefits of marine omega-3 fatty acids on cardiovascular disease end points. In the Vitamin D and Omega-3 Trial (VITAL), 840 mg/d of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) resulted in a 28% reduced risk for heart attacks, 50% reduced risk for fatal heart attacks, and 17% reduced risk for total coronary heart disease events. In the ASCEND trial (A Study of Cardiovascular Events in Diabetes), cardiovascular disease death was significantly reduced by 19% with 840 mg/d of EPA and DHA. However, the primary composite end points were not significantly reduced in either study. In REDUCE-IT (the Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial), there was a 25% decrease in the primary end point of major cardiovascular events with 4 g/d EPA (icosapent ethyl) in patients with elevated triglycerides (135-499 mg/dL) who also were taking a statin drug. For clinical practice, we now have compelling evidence of the cardiovascular benefits of omega-3 fatty acids. The findings of REDUCE-IT provide a strong rationale for prescribing icosapent ethyl for patients with hypertriglyceridemia who are on a statin. For primary prevention, the goal is to increase the population intake of omega-3 fatty acids to levels currently recommended, which translates to consuming at least one to two servings of fish/seafood per week. For individuals who prefer taking omega-3 fatty acid supplements, recent findings from clinical trials support the benefits for primary prevention.

TRIAL, YEAR	OMEGA-3 INTERVENTION	CONTROL	STUDY POPULATION	DURATION (YEARS)	PRIMARY OUTCOME(S)	
Diet and Reinfarction Trial (DART) 1989 [19,20]	Dietary advice to consume ≥2 servings of fatty fish per week Supplement subgroup: 3 g/d of fish oil (~840 mg/d EPA+DHA)*	No dietary advice	Men recovered from MI (N = 2,033)	2	Ischemic heart disease events (ischemic heart disease death and nonfatal MI) Total mortality	RR: 0.84 95% CI, 0.66-1.07 RR: 0.71 95% CI, 0.54-0.93
Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto micardico Prevenzione (GISSI-P) 1999 [21]	840 mg/d EPA+DHA as ethyl esters	Standard of care	Adults with previous MI in last 3 months (N = 11,323)	3.5	Death, nonfatal MI, nonfatal stroke CV death, nonfatal MI, nonfatal stroke	RR: 0.90 95% CI, 0.82-0.99 RR: 0.89 95% CI, 0.80-1.01
Japan EPA Lipid Intervention Study (JELIS) 2007 [22]	1,800 mg/d EPA as ethyl esters with statin	Statin only (no omega-3 fatty acids)	Adults with hypercholesterolemia, with or without a history of coronary artery disease (MI > 6 months) (N = 18,645)	4.6	Major coronary event (sudden cardiac death, fatal and nonfatal MI, and other nonfatal events)	HR: 0.81 95% CI, 0.69-0.95
Gruppo Italiano per lo Studio della Sopravvivenza nell'Insufficienza cardiaca-Heart Failure (GISSI-HF), 2008 [23]	840 mg/d EPA+DHA as ethyl esters	Unspecified placebo oil	Adults with chronic heart failure (N = 6,975)	3.9	All-cause mortality All-cause mortality or hospitalization for CVD	HR: 0.91 95.5% CI, 0.833-0.998 HR: 0.92 99% CI, 0.849-0.999
Alpha Omega 2010 [24]	Margarine containing 226 mg EPA and 150 mg DHA	Placebo or ALA-containing margarine	Adults with MI within 10 years (N = 4,837)	3.4	Major CV events (fatal and nonfatal cardiovascular events and cardiac interventions)	HR: 1.01 95% CI, 0.87-1.17
OMEGA 2010 [25]	840 mg/d EPA+DHA as ethyl esters	Olive oil placebo	Adults with acute MI (3-14 days) (N = 3,851)	1	Sudden cardiac death	OR: 0.95 95% CI, 0.56-1.60
Supplmentation en Folates et Omega-3 (SU.FOL.OM3) 2010 [26]	600 mg/d EPA+DHA at a ratio of 2:1	Placebo	Adults with acute coronary or cerebral ischemic event within < 1 year (N = 2,501)	4.7	Major CV events (composite of nonfatal MI, stroke, or death from CVD)	HR: 1.08 95% CI, 0.79-1.47
Outcome Reduction with an Initial Glargine Intervention (ORIGIN) 2012 [27]	840 mg/d EPA+DHA as ethyl esters	Olive oil placebo	Adults with CVD plus dysglycemia (N = 12,536)	6.2	Death from CVD	HR: 0.98 95% CI, 0.87-1.10
Risk and Prevention (R&P) 2013 [28,29]	840 mg/d EPA+DHA as ethyl esters	Olive oil placebo	Adults with high CVD risk without previous MI (N = 12,513)	5	Death or hospitalization from CVD	HR: 0.98 95% CI, 0.88-1.08
Age-Related Eye Disease Study 2 (AREDS2) 2014 [30]	350 mg DHA and 650 mg EPA	Corn oil placebo	Adults with intermediate or advanced age-related macular degeneration in one eye (N = 4,203)	4.8	CVD mortality (sudden death, death due to MI, heart failure, or stroke) and CVD morbidity (MI, stroke, unstable angina, coronary and carotid revascularization, hospitalized congestive heart failure, resuscitated cardiac arrest)	HR: 0.95 95% CI, 0.78-1.17

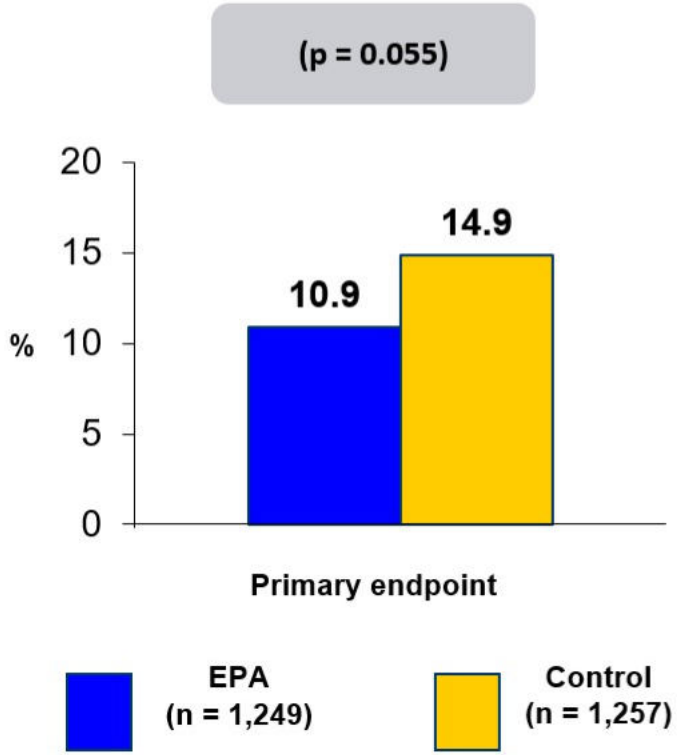
RANDOMIZED CONTROLLED TRIAL	COUNTRY	SAMPLE SIZE/SUBJECT TYPE	YEARS OF FOLLOW-UP	EPA+DHA DOSE	FINDINGS
ASCEND[5]	United Kingdom	15,480/patients with type 2 diabetes	7.4	840 mg	Composite end point not significantly altered Risk for vascular death ↓ by 19% (95% CI, 1%-33%)
VITAL[4]	United States	25,871/older adults without history of CVD or cancer	5.3	840 mg	Composite end point not significantly altered Risk for heart attack ↓ by 28% (95% CI, 10%-41%) Risk for total CHD ↓ by 17% (95% CI, 3%-29%)
REDUCE-IT[6]	International (11 countries)	8,179/statin-treated patients with median TG levels of 216 mg/dL and other CVD risk factors	4.9	3,600 mg (EPA only)	Primary CVD end point ↓ by 26% Significant reductions in several secondary end points

Table 1.
Comparison of three major trials of omega-3 fatty acids reported in 2018. ASCEND: A Study of Cardiovascular Events in Diabetes; VITAL: Vitamin D and Omega-3 Trial; REDUCE-IT (the Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial; CVD: cardiovascular disease; TG: triglycerides; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid; CHD: coronary heart disease

RESPECT-EPA

#AHA22

Trial Description: Patients with stable ischemic heart disease on statin therapy ≥1 month with plasma eicosapentanoic acid (EPA)/arachidonic acid (AA) ratio <0.4 were randomized by dynamic allocation to receive highly purified EPA (icosapent ethyl, 1800 mg/day) + statin vs. statin therapy alone. Follow-up was 5 years.



RESULTS

- Primary outcome, composite of CV death, nonfatal MI or stroke, unstable angina requiring revascularization, and other indicated coronary revascularization for EPA vs. control: 10.9% vs. 14.9% (p = 0.055)
- Sudden cardiac death, MI, unstable angina, or revascularization: 8.0% vs. 11.3%
- CV mortality: 2.0% vs. 3.0%
- Gastrointestinal disorders: 3.4% vs. 1.2%

CONCLUSIONS

- Results may have been underpowered due to lower-than-expected baseline event rate; however, they add to the findings of JELIS and REDUCE-IT trials supporting CV risk reduction with EPA administration
- Simultaneous prospective cohort study from the investigators will examine the utility of EPA/AA ratio as a biomarker of CV risk

Presented by Dr. Hiroyuki Daida at AHA Annual Scientific Sessions 2022

Developed by Dr. Amit Saha in collaboration with the *ACC.org* Editorial Board.

CLINICAL PRACTICE GUIDELINE

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

4.5.2. Hypertriglyceridemia

Recommendations for Hypertriglyceridemia
Referenced studies that support recommendations are summarized in Online Data Supplements 31 and 32.

COR	LOE	RECOMMENDATIONS
I	B-NR	1. In adults 20 years of age or older with moderate hypertriglyceridemia (fasting or nonfasting triglycerides 175 to 499 mg/dL [2.0 to 5.6 mmol/L]), clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes mellitus, chronic liver or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that increase triglycerides (S4.5.2-1).
IIa	B-R	2. In adults 40 to 75 years of age with moderate or severe hypertriglyceridemia and ASCVD risk of 7.5% or higher, it is reasonable to reevaluate ASCVD risk after lifestyle and secondary factors are addressed and to consider a persistently elevated triglyceride level as a factor favoring initiation or intensification of statin therapy (see Section 4.4.2.) (S4.5.2-2–S4.5.2-6).
IIa	B-R	3. In adults 40 to 75 years of age with severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL [≥5.6 mmol/L]) and ASCVD risk of 7.5% or higher, it is reasonable to address reversible causes of high triglyceride and to initiate statin therapy (S4.5.2-3–S4.5.2-5, S4.5.2-7, S4.5.2-8).
IIa	B-NR	4. In adults with severe hypertriglyceridemia (fasting triglycerides ≥500 mg/dL [≥5.7 mmol/L]), and especially fasting triglycerides ≥1,000 mg/dL (11.3 mmol/L)), it is reasonable to identify and address other causes of hypertriglyceridemia), and if triglycerides are persistently elevated or increasing, to further reduce triglycerides by implementation of a very low-fat diet, avoidance of refined carbohydrates and alcohol, consumption of omega-3 fatty acids, and, if necessary to prevent acute pancreatitis, fibrate therapy (S4.5.2-7, S4.5.2-9).

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VOL. 78, NO. 9, 2021

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EXPERT CONSENSUS DECISION PATHWAY

2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD Risk Reduction in Patients With Persistent Hypertriglyceridemia

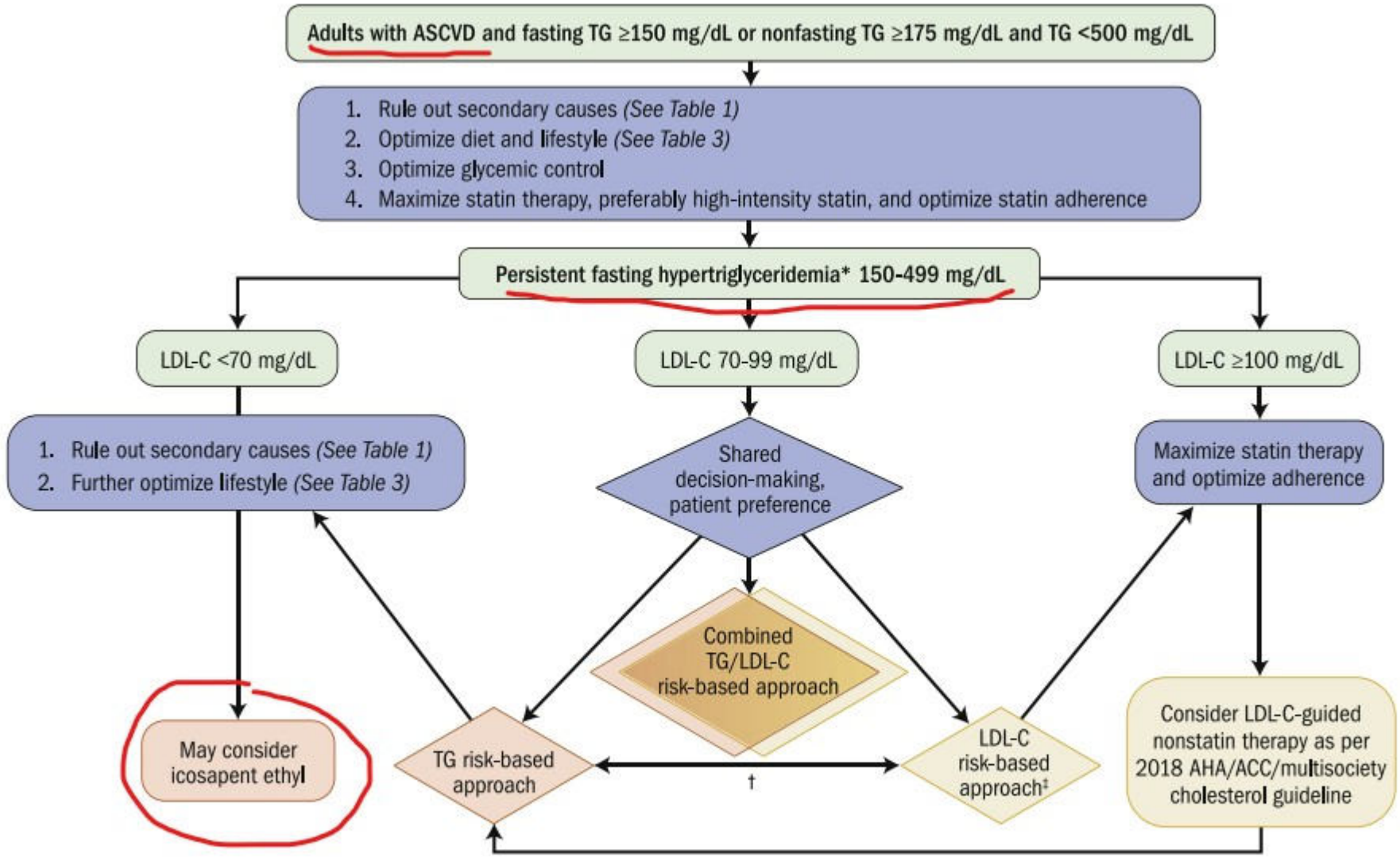
A Report of the American College of Cardiology Solution Set Oversight Committee

Endorsed by the National Lipid Association

TABLE 4 Summary of Nutrition Recommendations for Patients with Hypertriglyceridemia

	TG <500 mg/dL	TG 500-999 mg/dL	TG ≥1,000 mg/dL*	Patient Messages
Alcohol	Restrict Do not exceed limits: 2 drinks/d for men, 1 drink/d for women	Abstain completely	Abstain completely	For patients with TG <500 mg/dL, if alcohol is consumed, wine or beer with lower alcohol content is recommended over beverages with higher alcohol content. Alcohol content is listed on packaging and patients are encouraged to select beverages with lower alcohol content should they chose to consume alcohol.
Sugar-sweetened beverages	Restrict	Abstain completely	Abstain completely	Recommend plain or sparkling water, unsweetened tea, or coffee
Fruits†	Okay to include but individualize—3-4 servings/d	Limit to 3 or 4 servings/d and individualize. Avoid fruits with a high glycemic index (ie, pineapples, mangoes, watermelon, ripe bananas)	Limit to 1 serving/d. Recommend individualized medical nutrition therapy with a registered dietitian nutritionist	Consume whole fruit and avoid fruit juices when possible. Emphasize fresh fruits without added sugar or salt.
Vegetables	Emphasize vegetables	Emphasize vegetables, but avoid vegetables with a high glycemic index (ie, carrots, potatoes, sweet potatoes, yams, parsnips)	Emphasize vegetables, but avoid vegetables with a high glycemic index (ie, carrots, potatoes, sweet potatoes, yams, parsnips)	Avoid canned vegetables with salt and vegetables frozen with sauces. Avoid vegetable juices. Recommend 2.5 cups/d (77)‡
Legumes (beans, lentils, chickpeas, tofu, and so on)	Emphasize	Emphasize	Emphasize	Avoid added salt. Emphasize plant-based proteins instead of red meat. Avoid ultraprocessed meat alternatives.
Fish/seafood	Emphasize fatty fish Recommend at least 2 servings/wk	Emphasize either fatty or lean fish Recommend 2 (or more) servings/wk	Emphasize lean fish Recommend 2 (or more) servings/wk	Examples of fatty fish include salmon, farmed rainbow trout, and tuna. Examples of lean fish or seafood include cod, tilapia, haddock, flounder, and shrimp. Prioritize fresh, frozen, or packaged without sodium.

FIGURE 3 Adults With ASCVD and Fasting Triglycerides ≥150 mg/dL or Nonfasting Triglycerides ≥175 mg/dL and Triglycerides <500 mg/dL



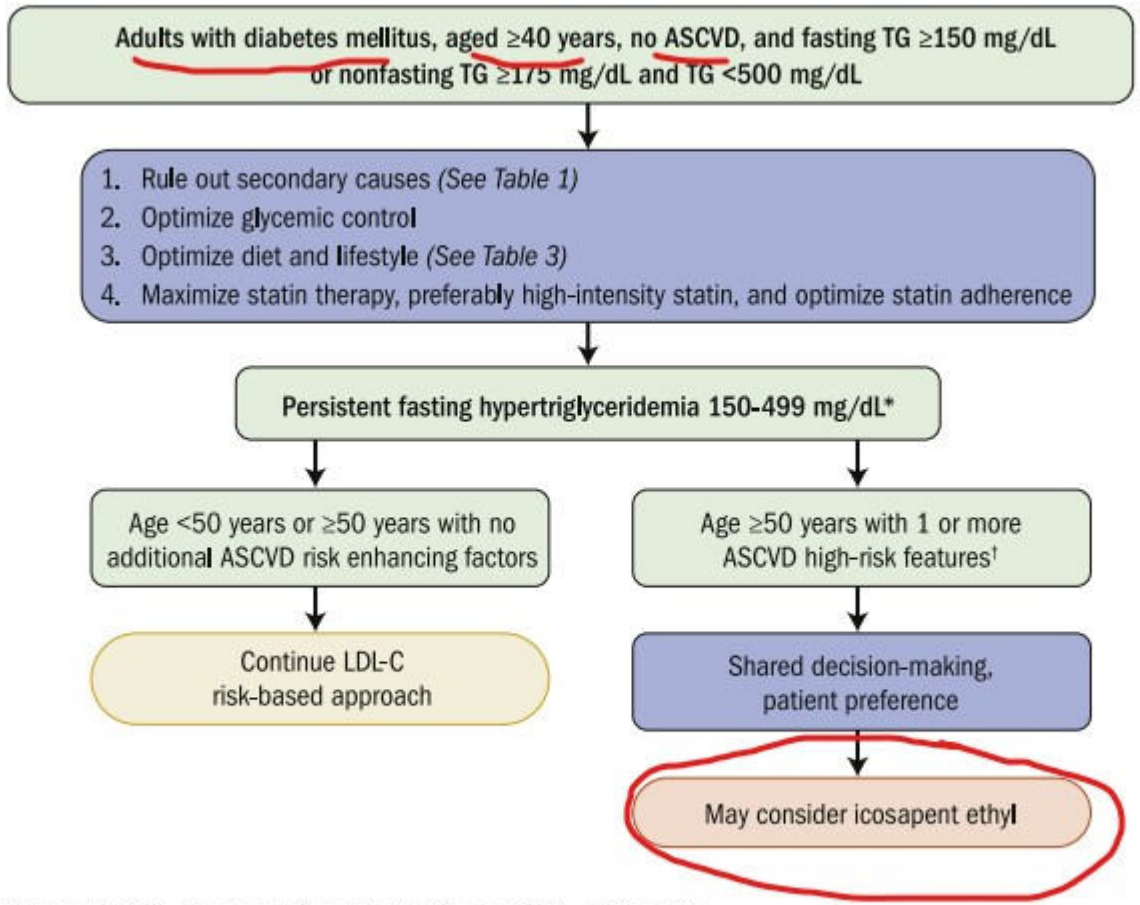
ACC = American College of Cardiology; AHA = American Heart Association; ASCVD = atherosclerotic cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; TG = triglycerides.

*Please refer to Section 4.7 for detailed definition.

†Clinicians could use a TG risk-based approach once LDL-C levels are optimized and vice versa.

‡Patients at very high risk are most likely to benefit from the addition of LDL-C risk-based nonstatin therapies.

FIGURE 4 Adults Aged ≥40 Years With Diabetes Mellitus, no ASCVD, and Fasting Triglycerides ≥150 mg/dL or Nonfasting Triglycerides ≥175 mg/dL and Triglycerides <500 mg/dL

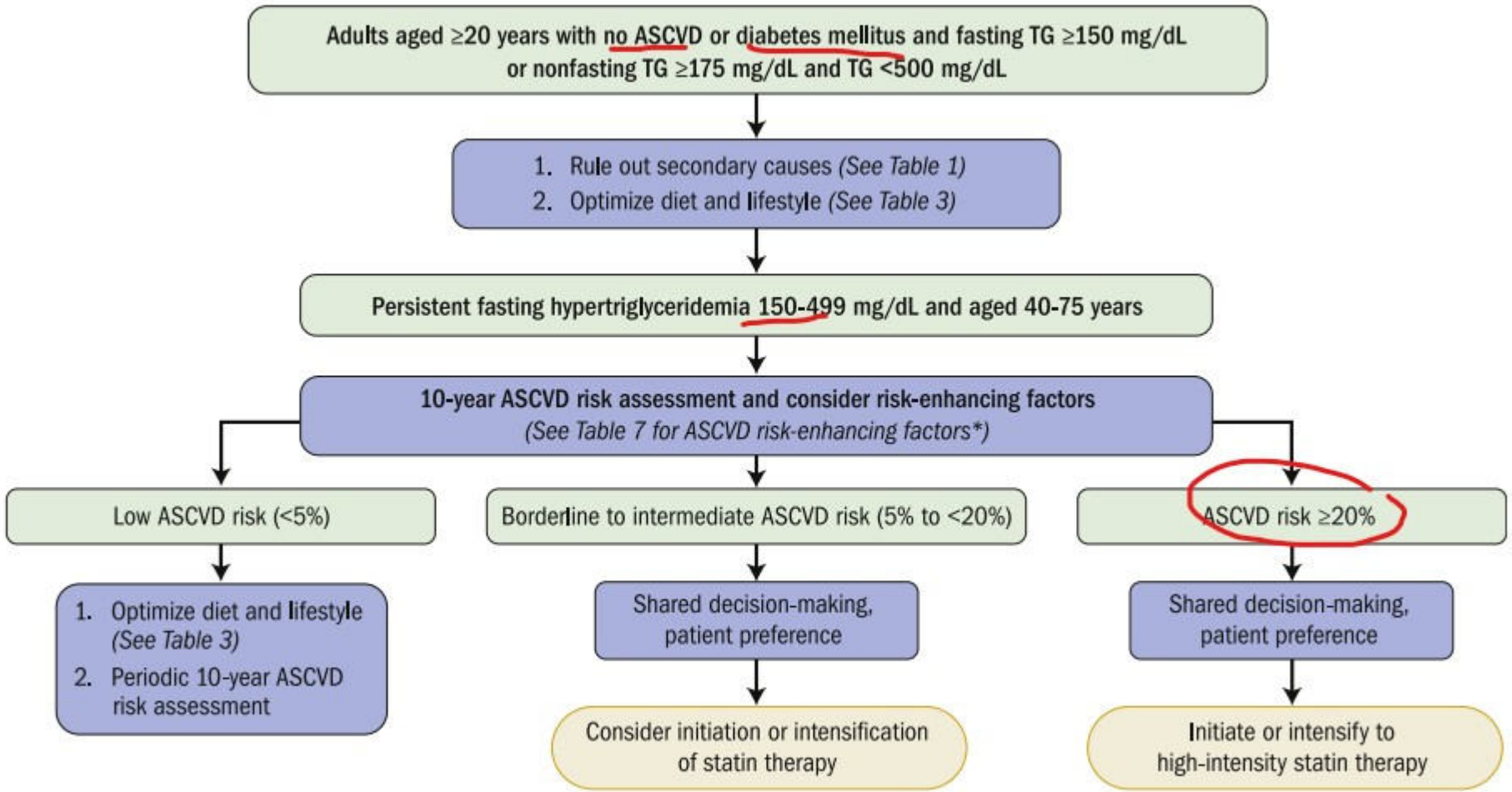


ASCVD = atherosclerotic cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; TG = triglycerides.

*Please refer to Section 4, Definition 1 for detailed definition of persistent hypertriglyceridemia.

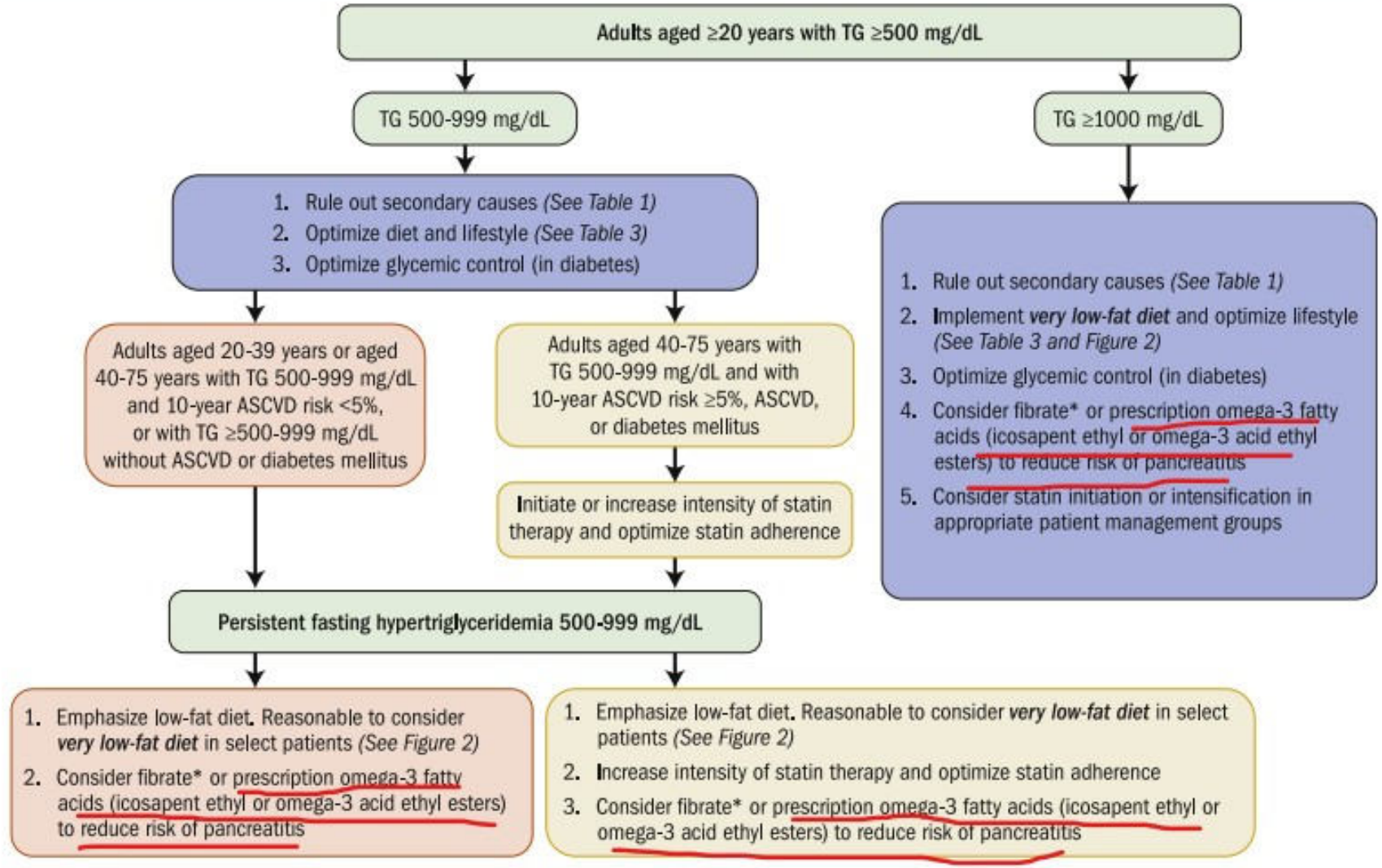
†As per REDUCE-IT inclusion criteria, high-risk features include: Men ≥55 years or women ≥65 years; cigarette smoking or stopped smoking within 3 months; hypertension (blood pressure ≥140 mm Hg systolic or ≥90 mm Hg diastolic) or on antihypertensive medication; high density lipoprotein cholesterol ≤40 mg/dL for men or ≤50 mg/dL for women; high sensitivity C reactive protein >3.0 mg/L (if measured); renal dysfunction: creatinine clearance >30 and <60mL/min; retinopathy; albuminuria (≥30 mcg of albumin/mg creatinine); ankle-brachial index <0.90 without symptoms of intermittent claudication (if measured).

FIGURE 5 Adults Aged ≥20 Years With No ASCVD or Diabetes Mellitus and Fasting Triglycerides ≥150 mg/dL or Nonfasting Triglycerides ≥175 mg/dL and Triglycerides <500 mg/dL



ASCVD = atherosclerotic cardiovascular disease; TG = triglycerides
*Use persistent hypertriglyceridemia as a risk enhancing factor

FIGURE 6 Adults Aged ≥20 Years With Severe Hypertriglyceridemia, Triglycerides ≥500 mg/dL, and Especially With Triglycerides ≥1,000 mg/dL



ASCVD = atherosclerotic cardiovascular disease; TG = triglycerides.

*Fenofibrate is the preferred fibric acid derivative due to better safety profile and fewer drug interactions compared to gemfibrozil.

Amerikan klavuzları özetle ne diyor?..

- Primer korumada (ASCVD ve DM yok),
  - *TG>500 mg/dl,
  - *özellikle pankreatit riski nedeni ile
  - *diyet ve yaşam tarzı değişikliği birlikte omega-3 alımı öneriyor..
  - *TG<500 mg/dl ise ilaç önermiyor..
- DM+ >50 yaş üstü+ en az bir tane yüksek ASCVD riski var,
  - *TG:150-500 mg/dl
  - * statin, yaşam tarzı değişikliği ve diyet ile düşmüyorsa omega-3 düşünülebilir.
- Sekonder korumada (ASCVD +)
  - *statin,yaşam tarzı değişikliği ve diyet ile düşmüyorsa
  - *Ayrıca LDL<70 mg/dl ise omega-3 düşünülebilir.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

ESC
European Society of Cardiology

EAS

Recommendations for drug treatments of patients with hypertriglyceridaemia (1)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia (TG >2.3 mmol/L (>200 mg/dL)).	I	B
In high-risk (or above) patients with TG between 1.5 and 5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2 x 2 g/day) should be considered in combination with statin.	IIa	B

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

ESC
European Society of Cardiology

Healthy diet characteristics (2)

Red meat should be reduced to a maximum of 350–500 g a week, in particular processed meat should be minimized
Fish is recommended 1–2 times per week, in particular fatty fish
30 g unsalted nuts per day
Consumption of alcohol should be limited to a maximum of 100 g per week
Sugar-sweetened beverages, such as soft drinks and fruit juices, must be discouraged
Red meat should be reduced to a maximum of 350–500 g a week, in particular processed meat should be minimized
Fish is recommended 1–2 times per week, in particular fatty fish

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

Recommendations for nutrition and alcohol

Recommendations	Class	Level
A healthy diet is recommended as a cornerstone of CVD prevention in all individuals.	I	A
It is recommended to adopt a Mediterranean or similar diet to lower risk of CVD.	I	A
It is recommended to replace saturated with unsaturated fats to lower the risk of CVD.	I	A
It is recommended to reduce salt intake to lower BP and risk of CVD.	I	A
It is recommended to choose a more plant-based food pattern, rich in fibre, that includes whole grains, fruits, vegetables, pulses, and nuts.	I	B
It is recommended to restrict alcohol consumption to a maximum of 100 g per week.	I	B
It is recommended to eat fish, preferably fatty, at least once a week and restrict (processed) meat.	I	B
It is recommended to restrict free sugar consumption, in particular sugar-sweetened beverages, to a maximum of 10% of energy intake.	I	B

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

Recommendations for drug treatments of patients with hypertriglyceridaemia

Recommendations	Class	Level
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia (triglycerides >2.3 mmol/L [200 mg/dL]).	I	A
In patients taking statins who are at LDL-C goal with triglycerides >2.3 mmol/L (200 mg/dL), fenofibrate or bezafibrate may be considered.	IIb	B
In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treatment and lifestyle measures, n-3 PUFAs (icosapent ethyl 2 x 2 g/day) may be considered in combination with a statin.	IIb	B

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

AVRUPA klavuzları özetle ne diyor?..

- Primer korumada diyetle omega-3 alımı önerilmekte..
- Sekonder korumada (yüksek ve çok yüksek riskli hastalar)

*statin, yaşam tarzı değişikliği ve diyete rağmen TG>135 mg/dl ise

* statine ilaveten n-3 PUFAs (icosapent ethyl 2x2 gr/gün) öneriliyor..

BALIK YAĞI

BALIK YAĞI TÜKETİMİ

- **Balık yağı tüketirken öncelikle alınan balık yağının ne kadar aktif madde (EPA+DHA) içerdiğine bakılmalıdır.**

- **Örneğin kapsül 500 mg'dır; ancak 100 mg aktif madde içeriyor olabilir.**

- **Sıvı preparatlar kapsüllere oranla çok daha fazla aktif madde içerirler.**

BALIK YAĞI TÜKETİMİ

- 1 balık yağı kapsülü ≈10 kkal enerji içermektedir.

1 balık yağı tabletinde;

- **En az 300 mg EPA, 150 mg DHA bulunmalıdır.**
- **EPA/DHA oranı: %60 olmalıdır.**

OMEGA-3 Kullanımında Dikkat Edilmesi Gereken Önemli Noktalar

- ✓ Ürünün etiketinde EPA ve DHA oranı mutlaka belirtilmiş olmalı.

- ✓ Omega-3 takviyelerinin içindeki EPA'nın DHA'ya oranı farklılık gösterir. Bu oran genellikle 2/3'tür.

(500 mg'lık bir kapsülde 300 mg EPA için 200 mg DHA bulunuyor anlamına gelir.)

- ✓ Omega-3'den en yüksek yararı elde etmek için Omega 6 içermeyen destekler tercih edilmelidir.

- ✓ Omega-3 yağları hava ile temasta okside olursa yapısı bozulur. Bu yüzden bu yağların içine konulan kapsüllerin hava sızdırmazlık özelliğinin olması gerekir.
- ✓ Cıva, kurşun ve diğer ağır metalleri içermediğine ilişkin IFOS sertifikasına sahip olması önemlidir.
- ✓ Kullanılacak Omega-3 desteğinin cıva, kurşun ve diğer ağır metalleri içermediğinden emin olmak için ürünün

  "The International Fish Oil Standards Program – IFOS" (Uluslararası Balık Yağı Standartları'na) uygun olup olmadığına bakılması gerekir.

Eve götürülecek mesajlar..

- Omega-3 ‘ün ilaç olarak kullanılmasının kardiyovasküler sonlanım noktalarına etkisi hala tartışmalı..
- Güçlü kanıtlara ihtiyaç var..
- Klavuzlarda daha çok omega-3’ün diyet ile alınması vurgulanmakta..
- Klavuzlarda ilaç olarak kullanılması kısıtlı endikasyonla ve zayıf öneri ile sunulmakta..
- Omega-3 den zengin deniz ürünleri (özellikle yağlı balık) haftada en az iki öğün tüketilmeli..
- Standartlara uygun balık yağı kullanılmasına dikkat edilmeli..

SABRINIZ

İÇİN

TEŞEKKÜRLER…..