Residueel cardiovasculair risico na acuut coronair syndroom

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Disclosure belangen S. van Wissen

(potentiële) belangenverstrengeling	Geen
Voor bijeenkomst mogelijk relevante relaties met bedrijven	
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk …	Consultaties voor Amgen, Sanofi, Daiichi Sankyo, Novartis, Bayer, Amarin, Alexion

Casus

- Patiënt van 64 jaar komt na ACS voor controle
- Patiënt heeft geen klachten bij controle
- Lab: glucose N 6.4 mmol/l, HbA1c 52 mmol/mol, kreat 86 mmol/l
- Lipidenprofiel: cholesterol 4.8, HDL 0.9, LDL 1.8, triglyceriden 4.3 mmol/l, cholesterol/HDL ratio 8
- Patiënt wordt behandeld met clopidogrel 75 mg, olmesartan 20 mg 1dd, amlodipine 5 mg, rosuvastatine 40 mg en ezetimibe 10 mg
- Wat is te doen met de lipiden?

Vraag

Met dit lipidenprofiel zou ik….

A. Niks doen

B. Iets doen

C. Nog geen idee, want daarvoor volg ik deze webinar

Vraag

U gaat wat doen en dan kiest u voor….

A. Fibraat starten

B. Bempedoïnezuur starten

C. Omega-3-visolie starten

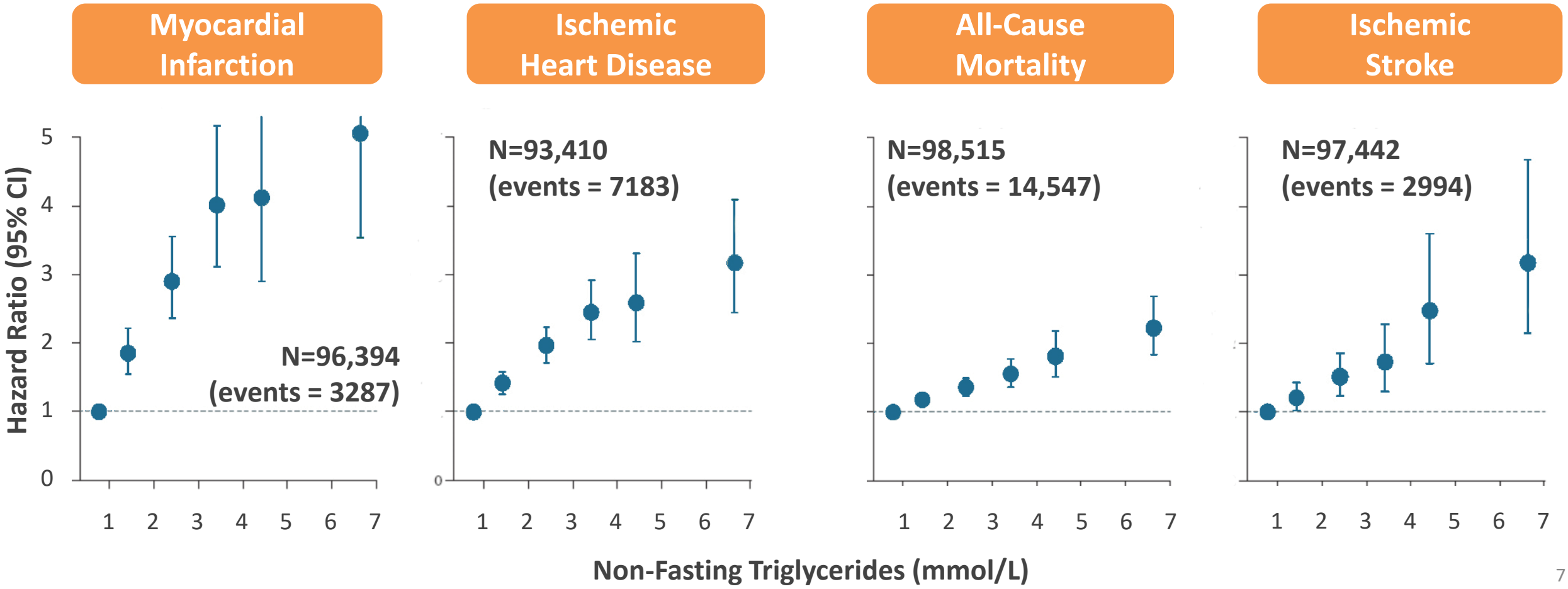
D. Icosapent-ethyl starten

Triglyceriden en residueel risico

- Volgens de richtlijn is het LDL op streefwaarde (<1.8 mmol/l)
- Triglyceriden zijn te hoog en HDL op de grens
- Verhoogde triglyceriden zijn een risicofactor voor hart- en vaatziekten

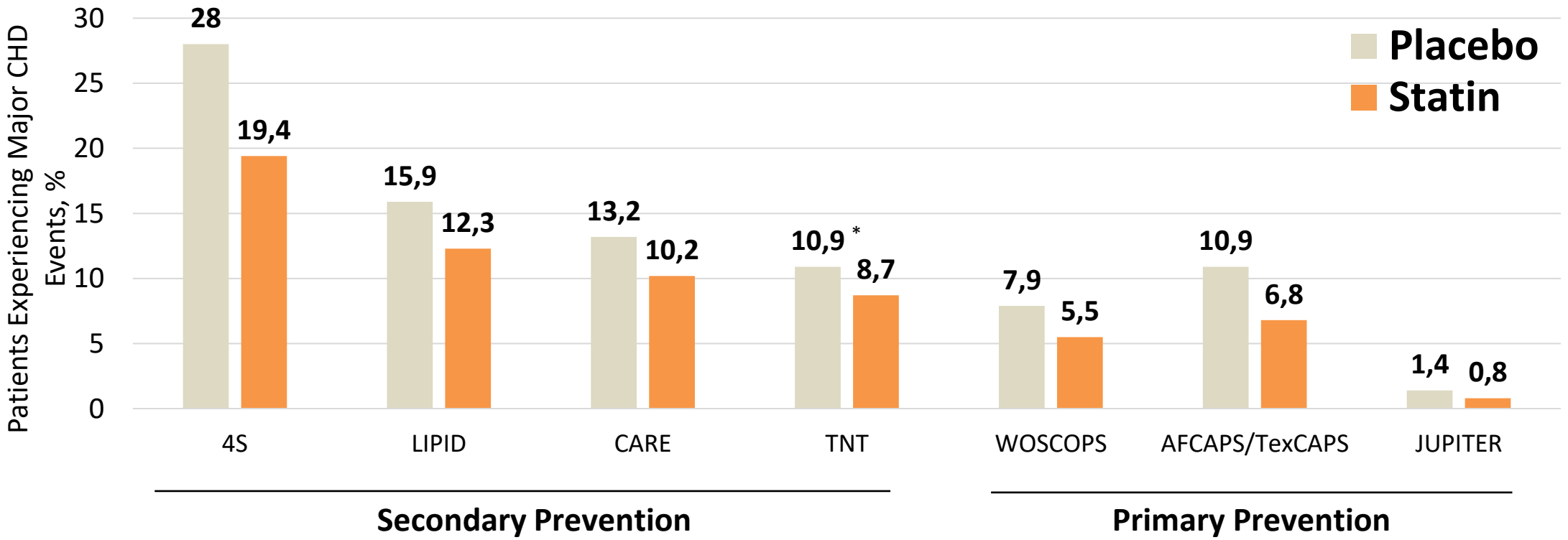
Elevated TGs Are Risk Markers of CV Risk and Mortality

Copenhagen City Heart Study and Copenhagen General Population Study



Nordestgaard BG, Varbo A. Lancet. 2014;384:626-635.

CV Events Remains High Despite Use of LDL-Lowering Therapies



On treatment LDL-C							
(mg/dL)	117	112	97	93	140	115	55
(mmol/L)	3.02	2.90	2.51	2.40	3.62	2.97	1.42

*, 10 mg atorvastatin was compared to 80 mg atorvastatin in the TNT trial.

1. 4S Group. Lancet. 1994;344:1383-9. 2. LIPID Study Group. N Engl J Med. 1998;339:1349-57. 3. Sacks FM et al. N Engl J Med. 1996;335:1001-9. 4. Sabatine MS. N Engl J Med 2017; 376:1713-1722. 5. Shepherd J et al. N Engl J Med. 1995;333:1301-7. 6. Downs JR et al. JAMA. 1998;279:1615-22. 7. Ridker PM et al. N Engl J Med. 2008;359:2195-207.

Wat te doen aan hoge triglyceriden?

TG-lowering therapies have not demonstrated CV benefit

TG-Lowering Agent	Key Trials*	Met 1° MACE Endpoint?
Fibrates	ACCORD[1] FIELD[2] PROMINENT[3]	✗
Niacin	AIM-HIGH[4] HPS2-THRIVE[5]	✗
Prescription and supplement, EPA + DHA mixtures	RISK & PREVENTION,[6] ORIGIN,[7] OMEGA,[8] ASCEND,[9] VITAL,[10] STRENGTH[11]	✗

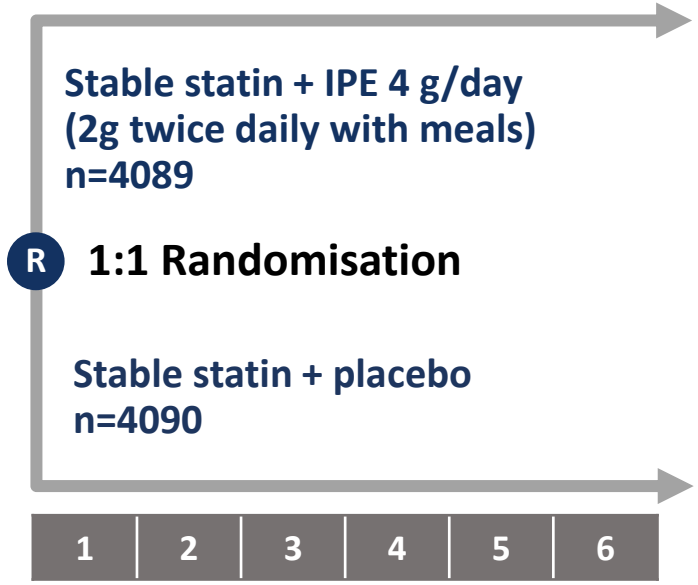
*ACCORD: Action to Control Cardiovascular Risk in Diabetes; AIM-HIGH: Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes; ASCEND: A Study of Cardiovascular Events in Diabetes; FIELD: Fenofibrate Intervention and Event Lowering in Diabetes; HPS2-THRIVE: Heart Protection Study 2–Treatment of HDL to Reduce the Incidence of Vascular Events; OMEGA: Effect of Omega 3-Fatty Acids on the Reduction of Sudden Cardiac Death After Myocardial Infarction; ORIGIN: Outcome Reduction with an Initial Glargine Intervention; PROMINENT: Pemafibrate to Reduce Cardiovascular OutcoMes by Reducing Triglycerides IN patiENts With diabetes; STRENGTH: Statin Residual Risk with Epanova in High Cardiovascular Risk Patients with Hypertriglyceridemia; VITAL: Vitamin D and Omega-3 Trial.

DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid

1. ACCORD Study Group. *N Engl J Med.* 2010;362(17). ***2.*** FIELD Study Investigators. *Lancet*. 2005;366(9500). **3.** PROMINENT Study group. *N Engl J Med.* 2022 DOI: 10.1056 **4.** AIM-HIGH Investigators. *N Engl J Med*. 2011;365(24).
5. HPS2-THRIVE Collaborative Group. *N Engl J Med*. 2014;371(3). **6.** Risk and Prevention Study Collaborative Group. *N Engl J Med*. 2013;368(19). **7.** ORIGIN Trial Investigators. *N Engl J Med*. 2012;367(4).
8. OMEGA Study Group. *Circulation*. 2010;122(21). **9.** ASCEND Study Collaborative Group. *N Engl J Med*. 2018;379(16). **10.** Manson JE, et al. *N Engl J Med*. 2019;380(1). **11.** Nicholls SJ et al. *JAMA.* 2020;324(22).

REDUCE-IT: A multi-center, randomized, double-blind, placebo-controlled, event-driven trial[1,2]

- 473 study centres
- 11 countries



Median trial follow-up: 4.9 years

Primary Endpoint

Time to first 5-point composite MACE:

- CV death
- Non-fatal MI
- Non-fatal stroke
- Coronary revascularisation
- Hospitalisation for unstable angina

Key Secondary Endpoint

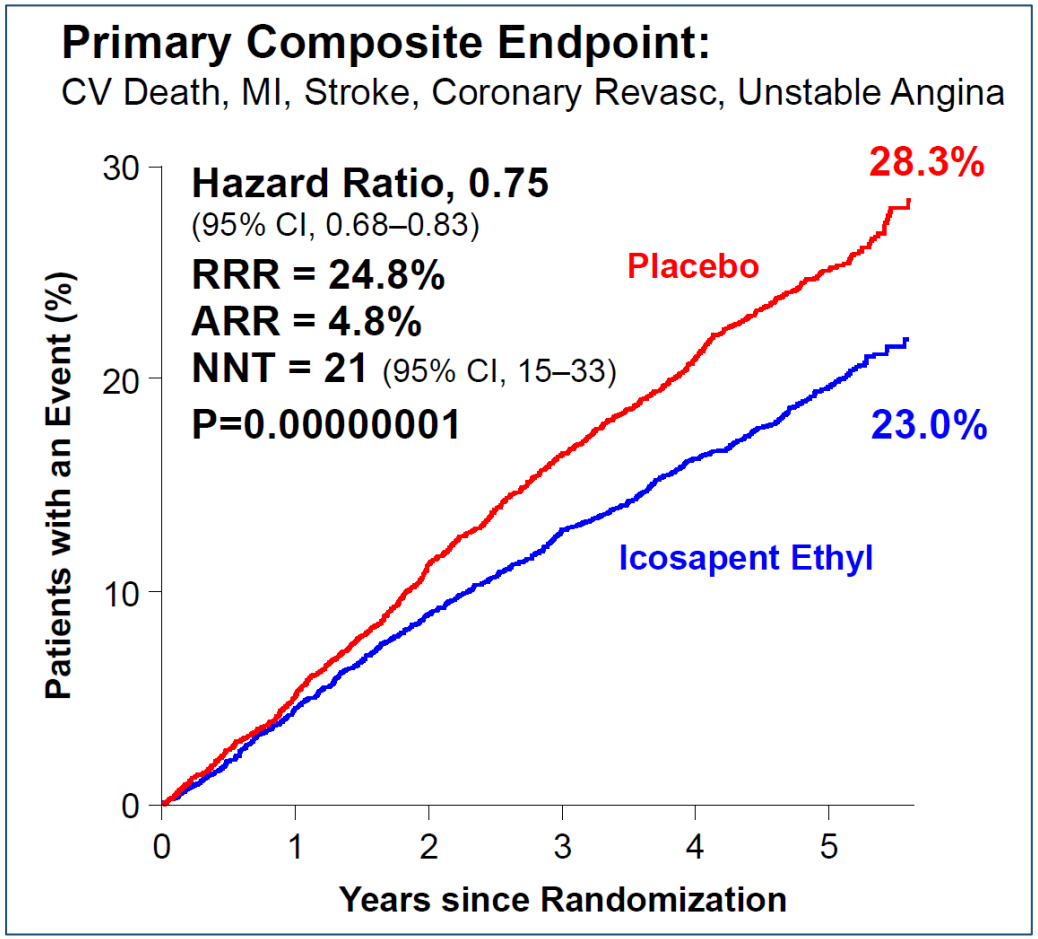
Time to first 3-point composite MACE:

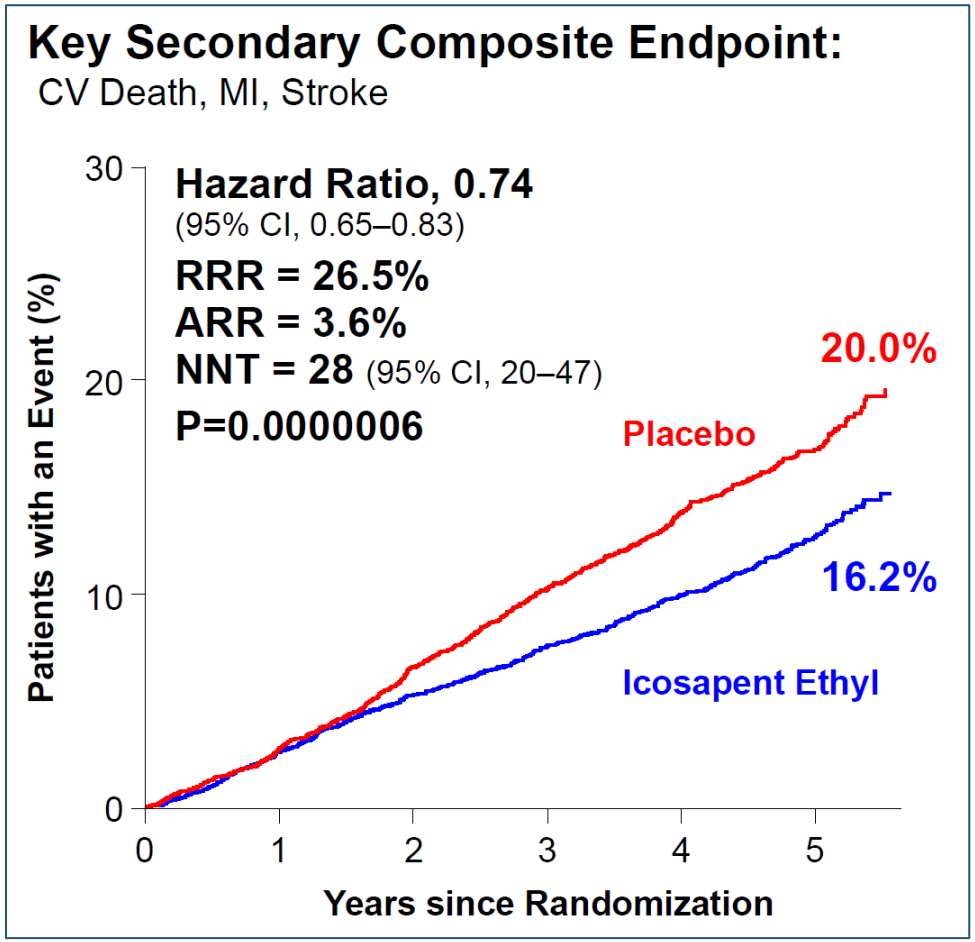
- CV death
- Non-fatal MI
- Non-fatal stroke

IPE: icosapent ethyl

1. Bhatt DL et al. *Clin Cardiol*. 2017;40(3); **2**. Bhatt DL et al. *N Engl J Med*. 2019;380(1).

Primary and key secondary endpoints

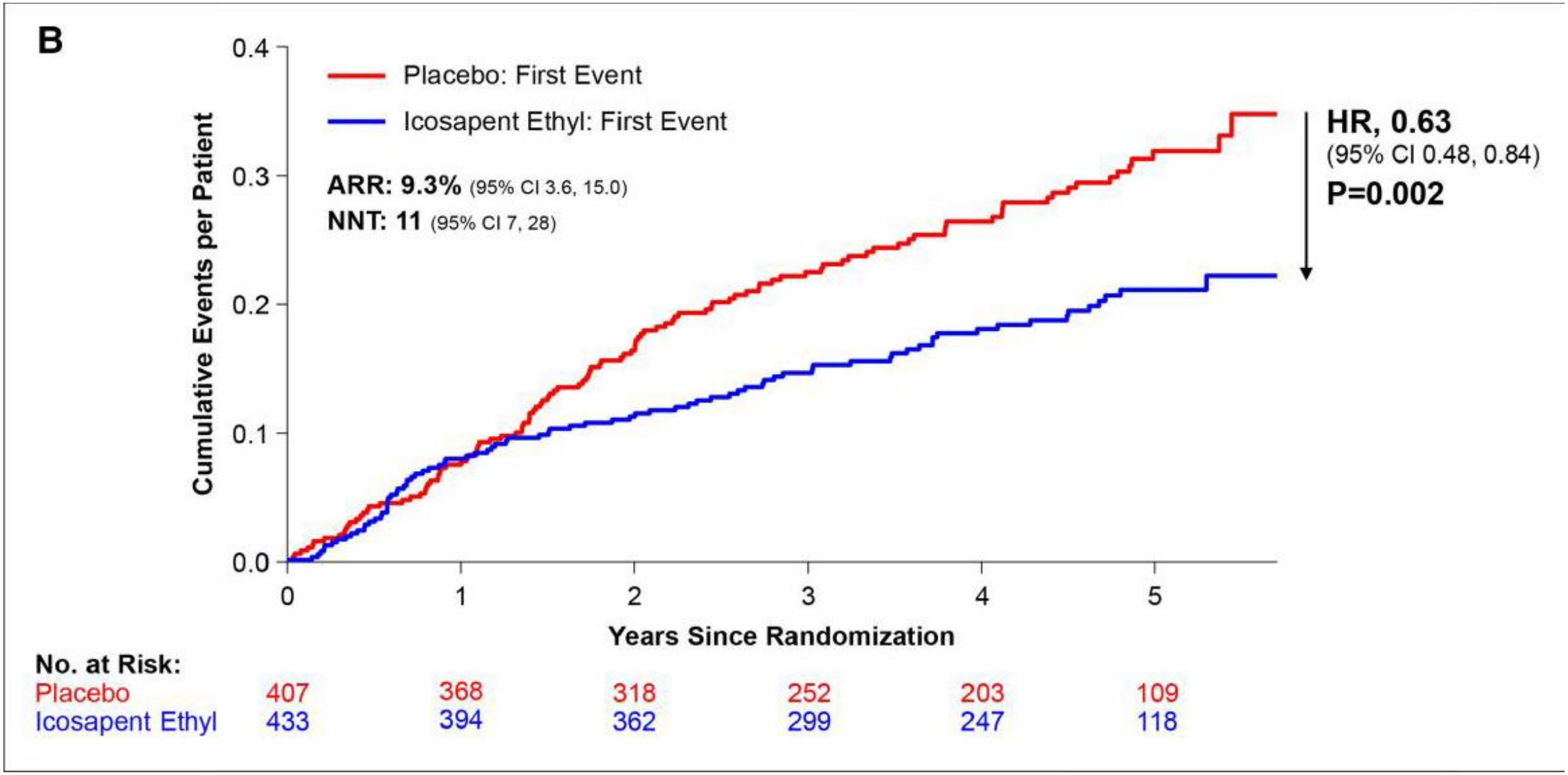




Kaplan–Meier event curves for the primary and key secondary efficacy endpoint in a time-to-event analysis

Bhatt DL et al. *N Engl J Med.* 2019;380(1).

Icosapent ethyl following acute coronary syndrome

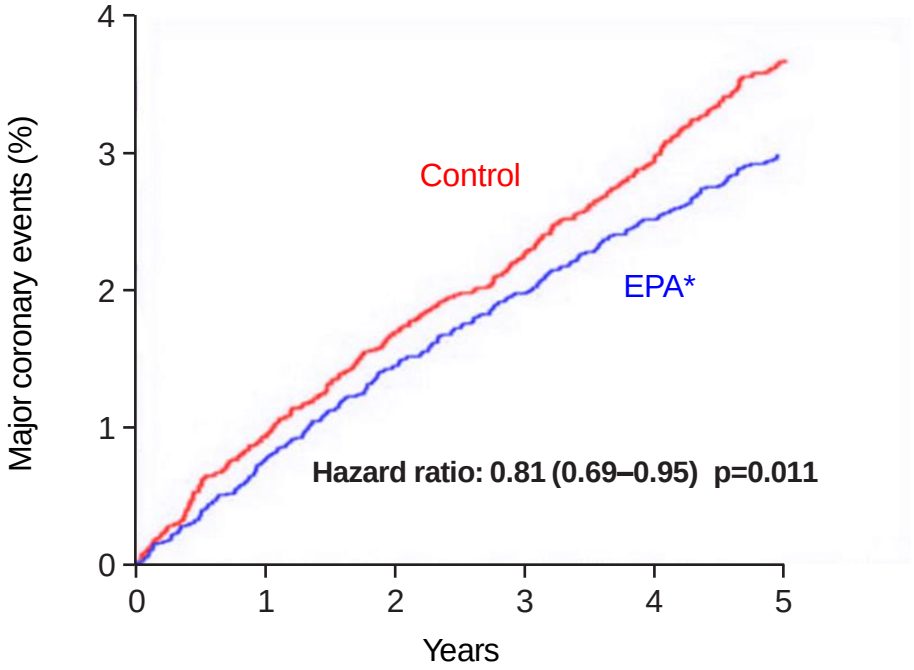


Sayah N, et al. Eur Heart J 2024, Jan 22

Wat valt op in deze studie?

Recent large outcome trials using high dose Omega-3 fatty acids

JELIS [1]

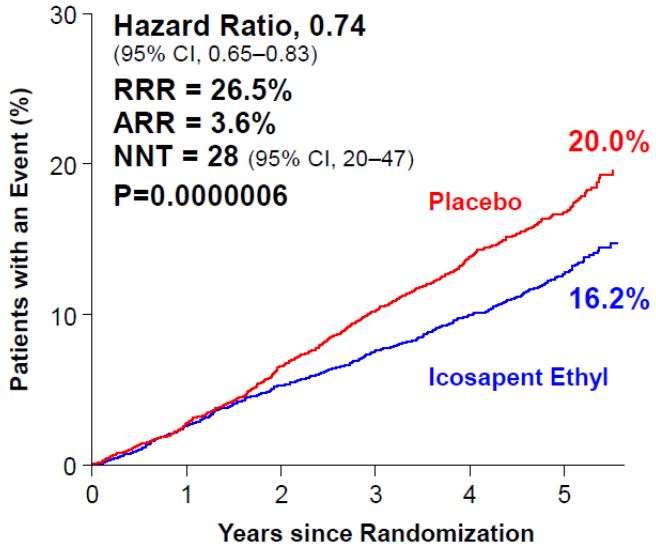


1.8 g EPA

No placebo

REDUCE IT [2]

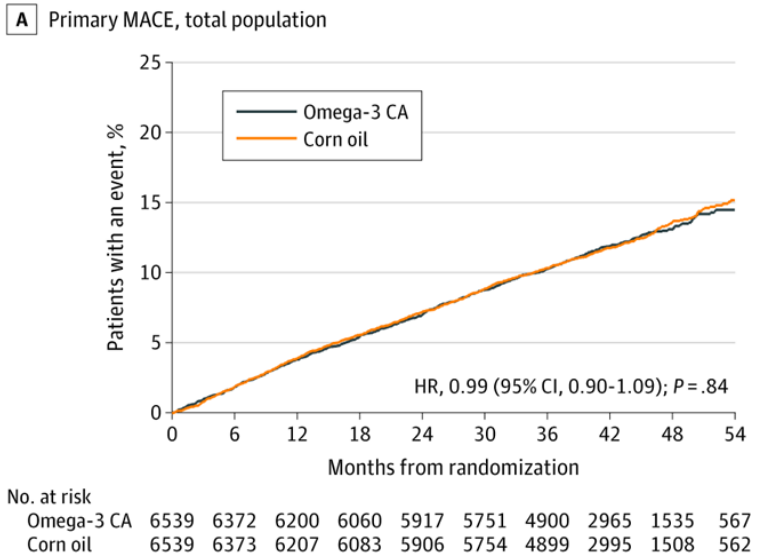
CV death/MI/Stroke



4 g EPA

Mineral oil placebo

STRENGTH [3]



4 g EPA and DHA

Corn oil placebo

1. Yokoyama M, et al. *Lancet*. 2007;369(9567). 2. Bhatt DL et al. *N Engl J Med.* 2019(1) 3. Nicholls SJ, et al. *JAMA*. 2020.

A proprietary purification process of icosapent ethyl

Majority of Fish Oil Supplements*
EPA 18%
DHA 12%

EPA 26%
DHA 16%

EPA 65%
DHA <5%

Icosapent-Ethyl
≥EPA 96%
DHA Not Detected

IPE PURITY

**Based on fish oil capsules containing 18% EPA, 12% DHA, and 70% other undisclosed fatty acids*

DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid; IPE: icosapent ethyl.

Data on file (VAS-01751).

Wat valt op wat betreft bijwerkingen?

Safety and tolerability

The most frequently reported adverse reactions with icosapent ethyl were bleeding (11.8%), peripheral oedema (7.8%), atrial fibrillation (5.8%), constipation (5.4%), musculoskeletal pain (4.3%), gout (4.3%) and rash (3.0%).

		Icosapent ethyl (n=4089)	Placebo (n=4090)
Bleeding*		11.8%	9.9%
	Serious bleeding in combination with antithrombotic medication	3.4%	2.6%
	Serious bleeding without taking antithrombotic medication	0.2%	0.2%
Atrial fibrillation/flutter**		5.8%	4.5%
	Requiring hospitalization for 24 hours or more	3%	2%

*The bleeding events most frequently observed with icosapent ethyl were gastrointestinal bleeding (3.1%), contusion (2.5%), haematuria (1.9%) and epistaxis (1.5%)
** In patients that had a previous history of atrial fibrillation/flutter , atrial fibrillation/flutter was reported more frequently in the icosapent ethyl group (12.5%) than in the placebo group (6.3%) without statistical interaction (interaction p-value = 0.21)

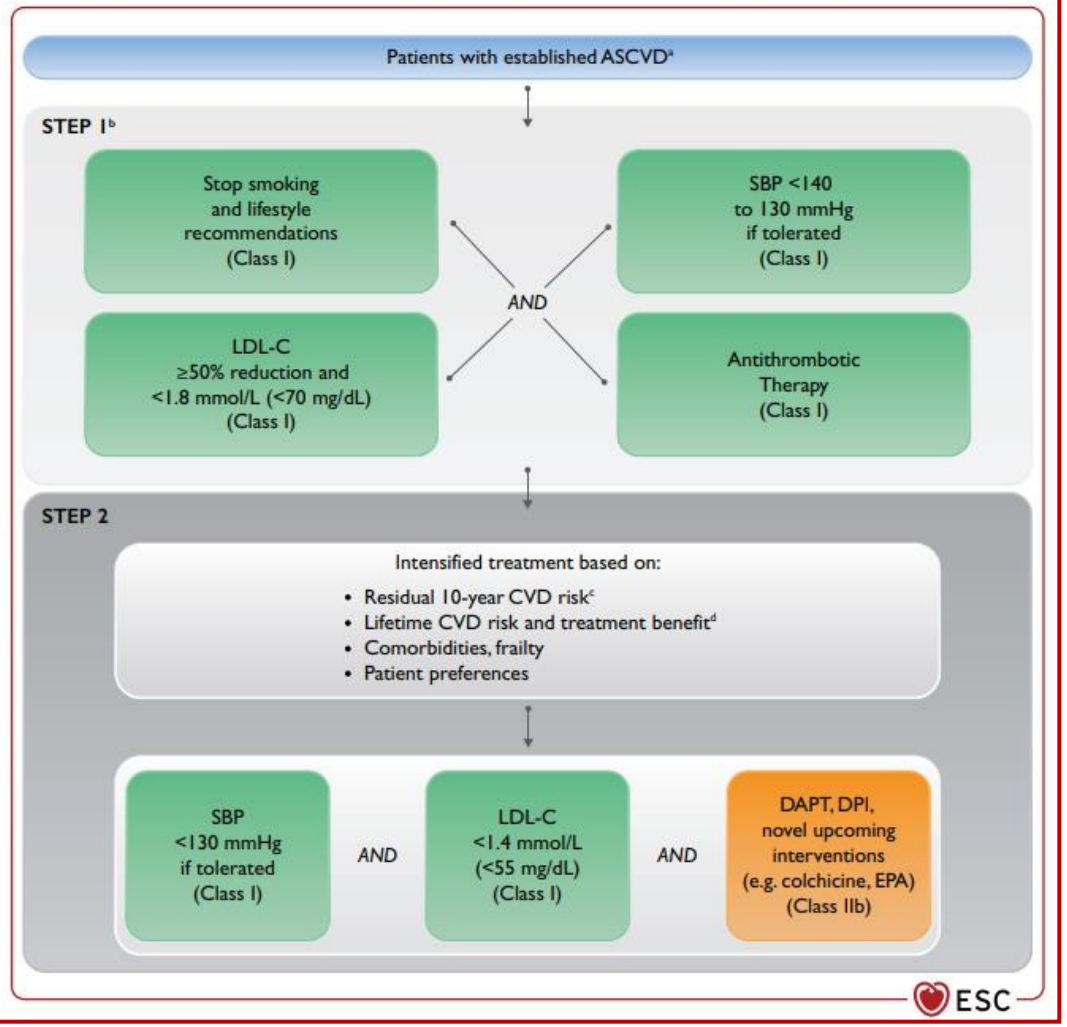
SmPC Icosapent ethyl

Wanneer toe te passen?

ESC guidelines: recommendations for use of icosapent ethyl

Recommendations for drug treatments of patients with hypertriglyceridaemia.

Recommendations	Class[a]	Level[b]
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)].[533]	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.[534–536]	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 × 2 g/day) may be considered in combination with a statin.[84]	IIb	B



ESC guidelines on CVD prevention 2021[1]

1. Visseren F et al. *Eur Heart J.* 2021.

Vergoeding icosapent-ethyl

- Patiënten met een vastgestelde cardiovasculaire aandoening (zoals ACS)
- Patiënten met een triglyceriden tussen 1.7 en 5.6 mmol/l onder een statine
- Dan capsules 2dd2 met 998 mg icosapent-ethyl

Terug naar de casus

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- Patiënt heeft geen klachten bij controle
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Conclusies

- Residueel risico risico op hart- en vaatziekten is nog een uitdaging
- Meerdere oorzaken voor residueel risico
- Belangrijk zijn hoog triglyceriden (en laag HDL) en inflammatie
- Bij hoog risico patiënt is behandeling met EPA een optie

Dank voor uw aandacht

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