

ALPHA OMEGA:

Effect of low doses of n-3 fatty acids on cardiovascular diseases in post-MI patients

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GRANTS

- Netherlands Heart Foundation,
The Hague, The Netherlands



- National institutes of Health,
Bethesda MD, U.S.A.



- Unilever, Vlaardingen, The Netherlands



- Presenter disclosure: no conflicts of interest

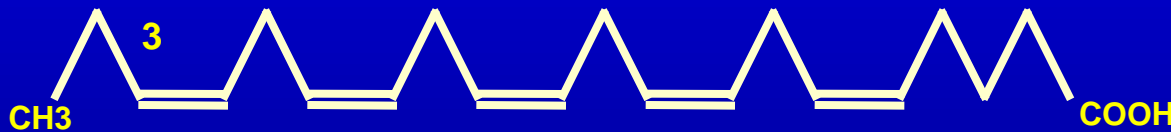
TRIAL CONDUCT

- Investigator-initiated study
- Study design, conduct and reporting are solely those of the Alpha Omega Trial Group
- Data-analysis by independent statistician

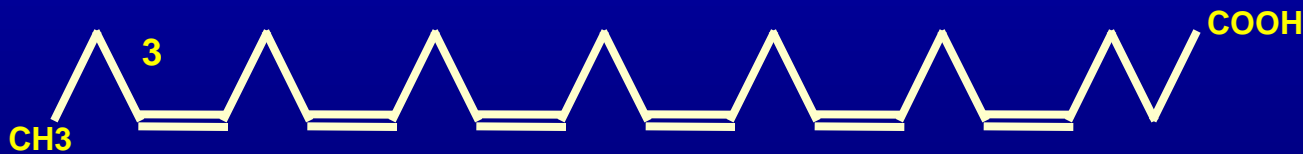
N-3 FATTY ACIDS




Alpha-linolenic acid (ALA, C18:3n-3)



Eicosapentaenoic acid (EPA, C20:5n-3)



Docosahexaenoic acid (DHA, C22:6n-3)



Limited conversion
in humans (<10%)

HYPOTHESES

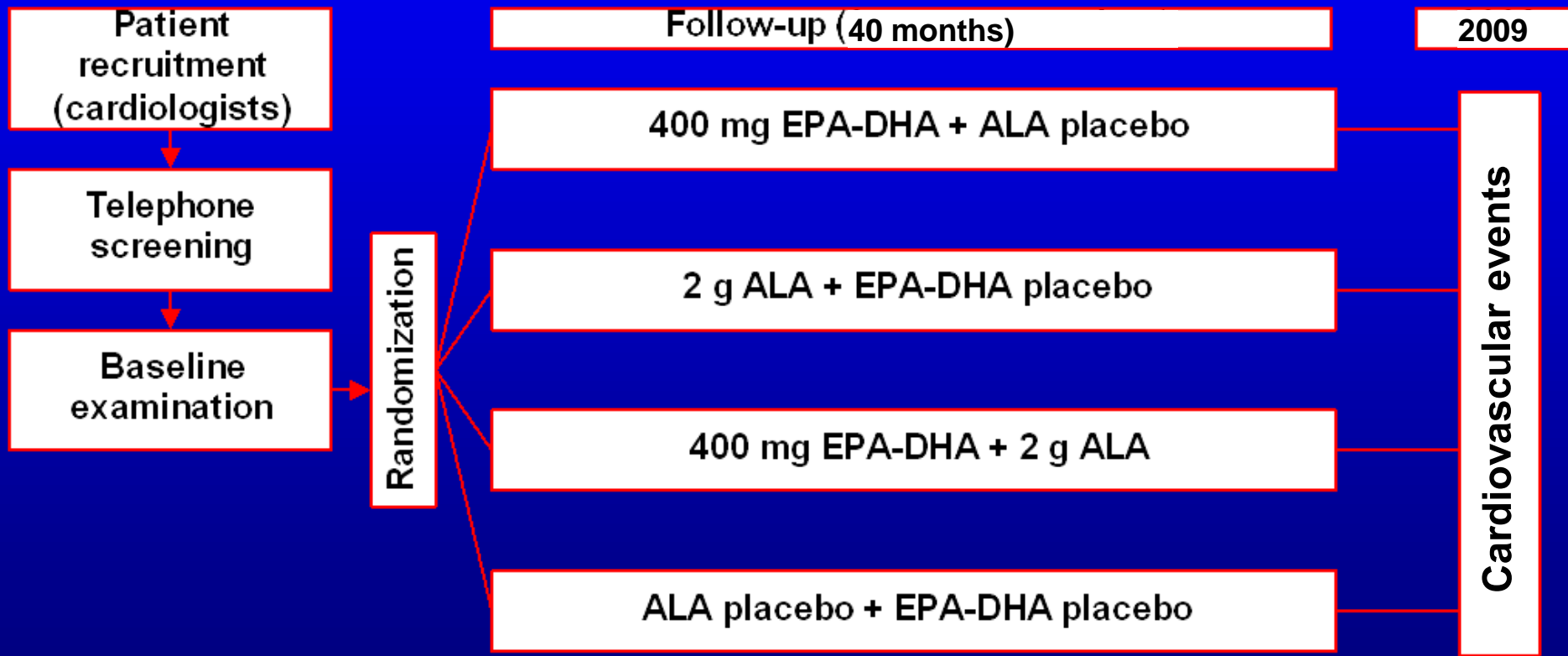
N-3 fatty acids reduce the risk of:

- major cardiovascular events
- fatal coronary heart disease
- ventricular arrhythmia-related events

PATIENT CHARACTERISTICS

	EPA+DHA and ALA n=1212	EPA+DHA n=1192	ALA n=1197	Placebo n=1236
Age, y	69 ± 6	69 ± 6	69 ± 6	69 ± 6
Men, %	78	78	78	79
Time since MI, y	4.2 ± 3.1	4.3 ± 3.2	4.4 ± 3.3	4.3 ± 3.3
Diabetes mellitus, %	20	22	22	20
Cardiovascular medication, %				
Antithrombotic agents	96	98	98	98
BP lowering drugs	90	91	88	89
Lipid lowering drugs	87	85	86	85
Antiarrhythmic drugs	3	3	3	3
Systolic blood pressure, mmHg	141 ± 22	142 ± 22	141 ± 21	142 ± 22
Serum total cholesterol, mmol/l	4.7 ± 1.0	4.8 ± 1.0	4.7 ± 1.0	4.8 ± 1.0
Body mass index, kg/m ²	27.8 ± 4.0	27.7 ± 3.7	27.8 ± 3.8	27.8 ± 3.9
Current smoker, %	15	17	17	18

DESIGN ALPHA OMEGA TRIAL



TRIAL MARGARINES

Use of trial margarine on bread 20 grams per day
≈ 3-4 slices of bread

Daily doses of n-3 fatty acids in the 4 groups:

I: 400 mg EPA+DHA

II: 2 g ALA

III: 400 mg EPA+DHA and 2 g ALA

IV: 0 mg EPA+DHA, 0 mg ALA



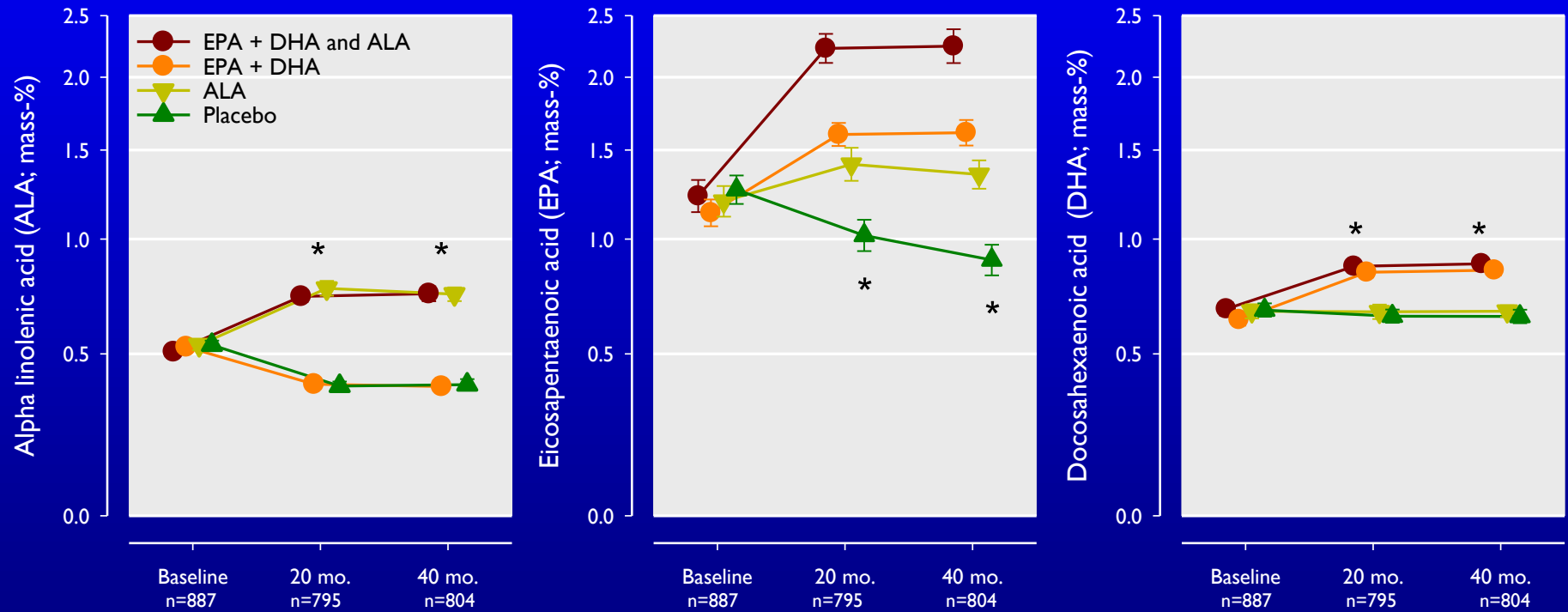
PARTICIPATING CENTERS

Centers are listed at www.alphaomegatrial.com



COMPLIANCE

Change in plasma n-3 fatty acids during the trial



* P < 0.001

ENDPOINTS

Primary outcome

Major cardiovascular events:

fatal and non-fatal cardiovascular events and cardiac interventions (PCI, CABG)

Secondary outcomes

Incidence of cardiovascular diseases

Fatal cardiovascular diseases

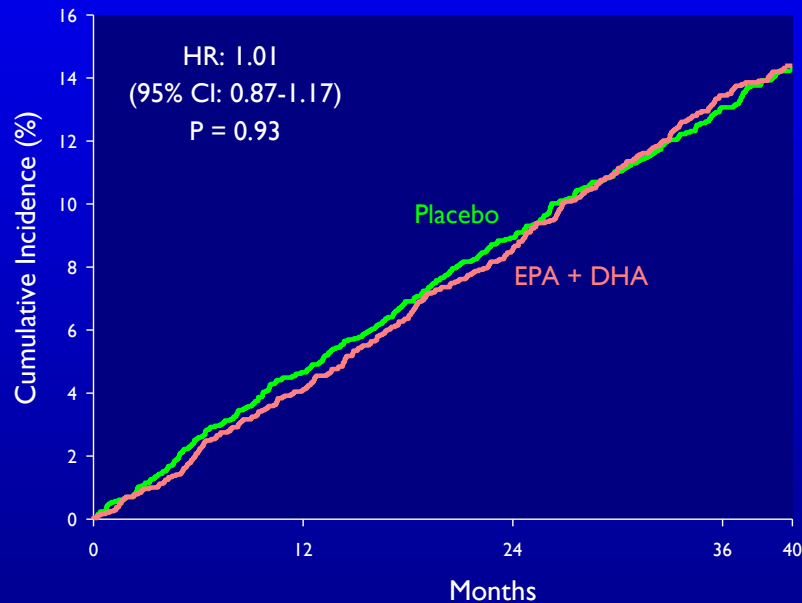
Fatal coronary heart disease

Ventricular arrhythmia-related events: sudden death, cardiac arrest and placement of implantable cardioverter-defibrillator

Death from any cause

EPA+DHA AND ENDPOINTS

Major Cardiovascular Events



Secondary outcomes:

Incident CVD

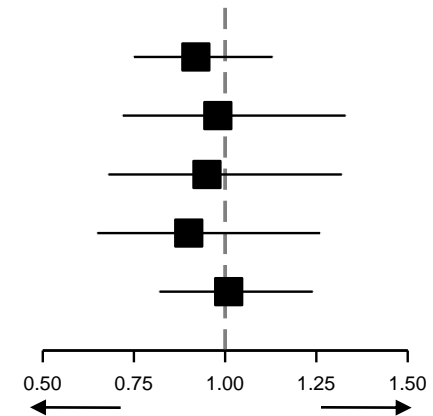
Fatal CVD

Fatal CHD

Ventr. arrhythmia-related events

Death from any cause

Hazard ratio (95% CI)



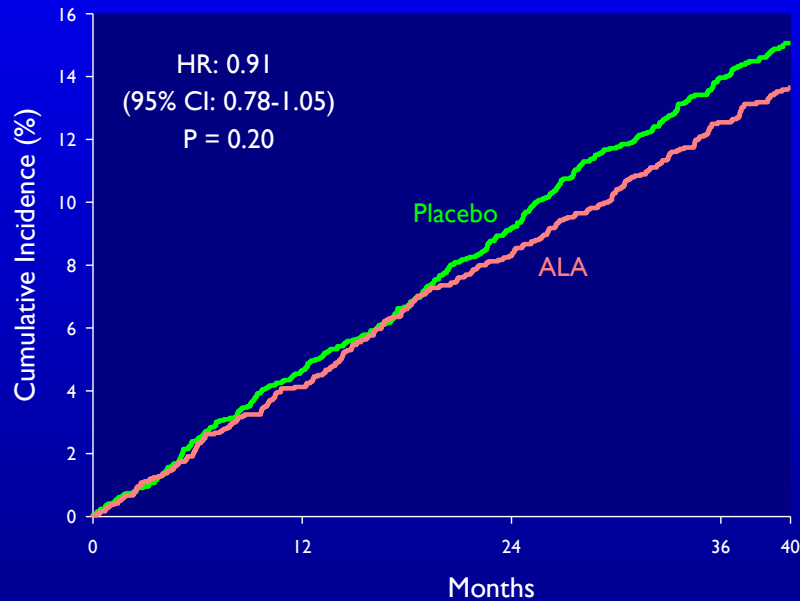
EPA+DHA better

Placebo better

Findings were similar in men and women

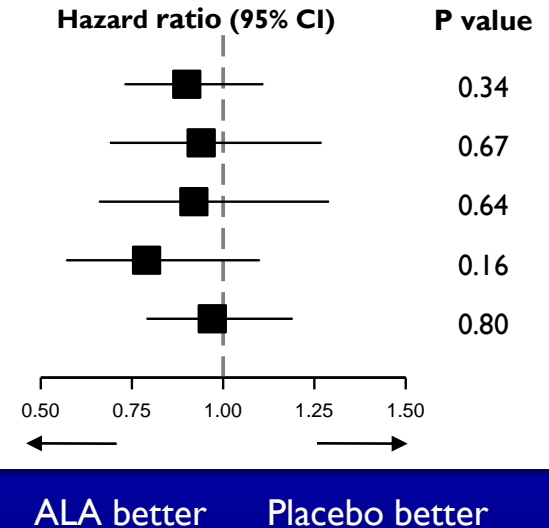
ALA AND ENDPOINTS

Major Cardiovascular Events



Secondary outcomes:

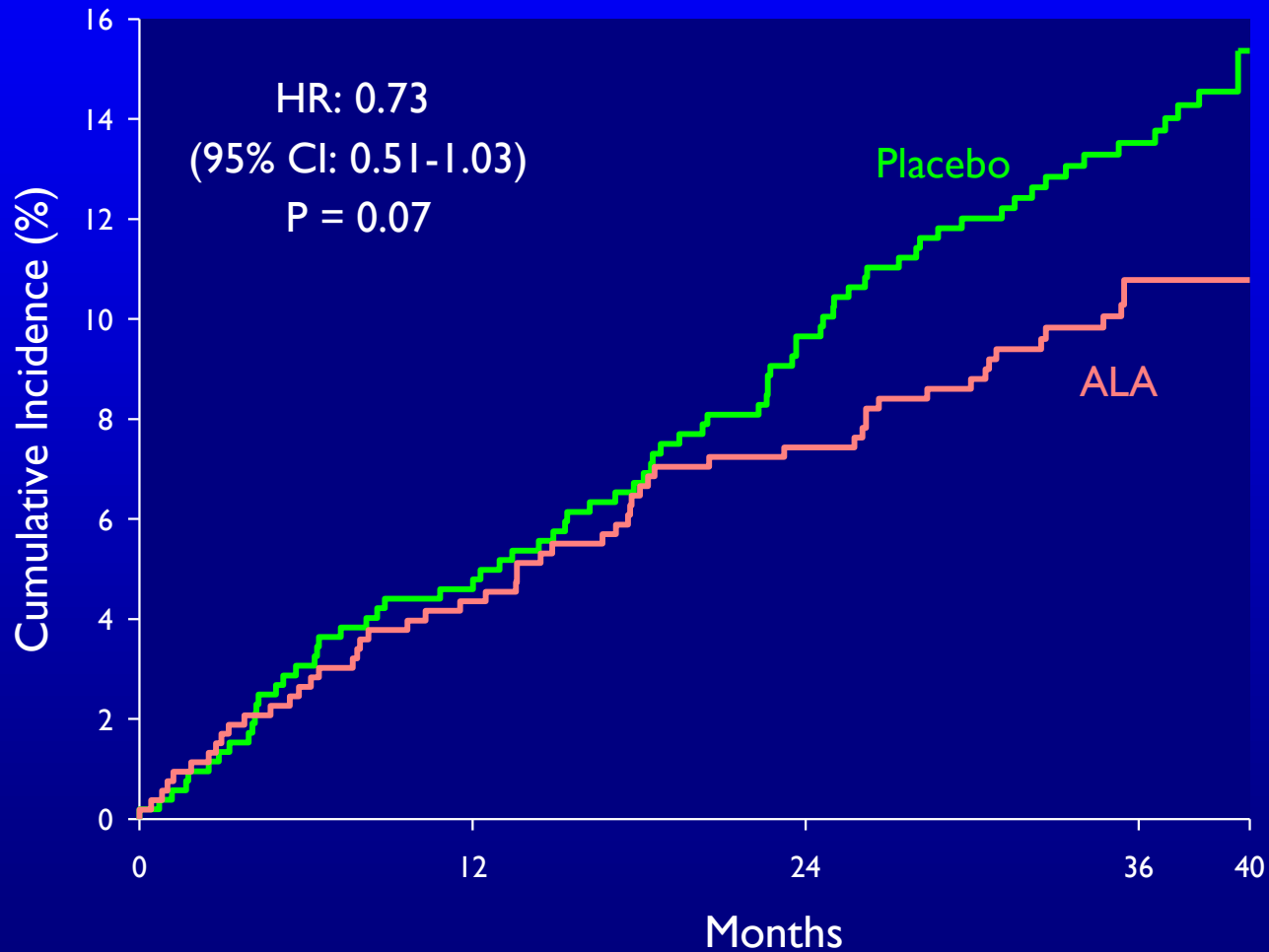
- Incident CVD
- Fatal CVD
- Fatal CHD
- Ventr. arrhythmia-related events
- Death from any cause



Findings differed between men and women

RESULTS IN WOMEN

Major Cardiovascular Events



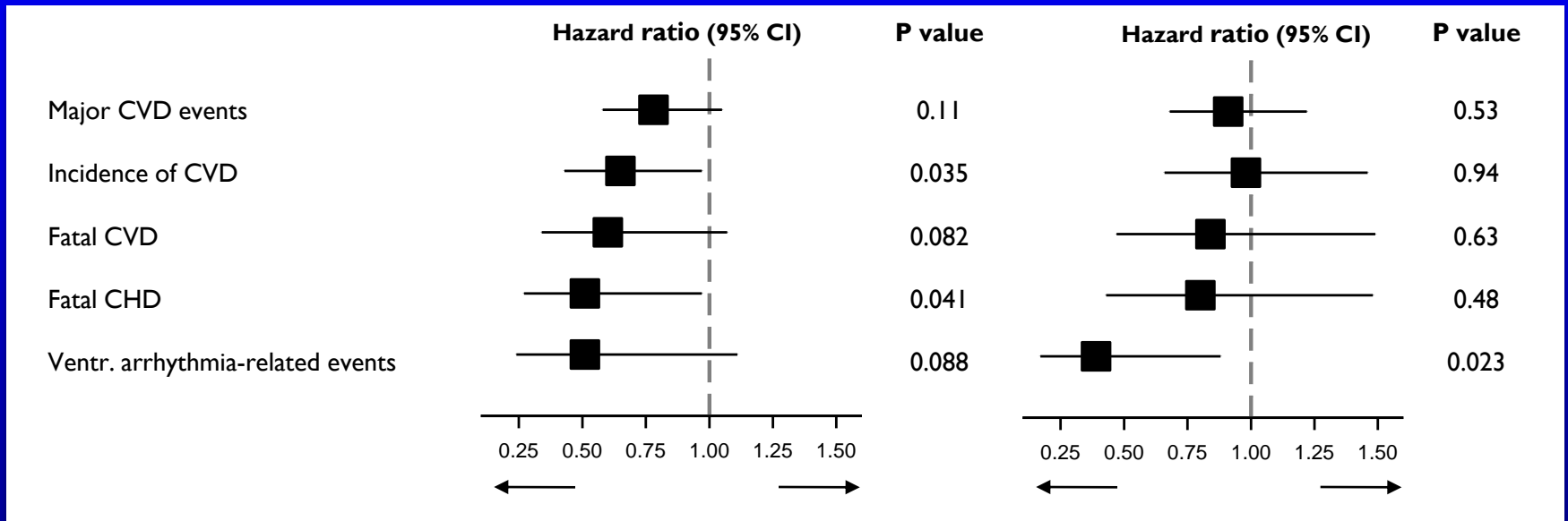
Post-hoc analysis

Patients with diabetes (n=1,014) had 30% higher risk of major cardiovascular events than non-diabetics (n=3,823)

RESULTS IN DIABETIC PATIENTS

EPA+DHA

ALA



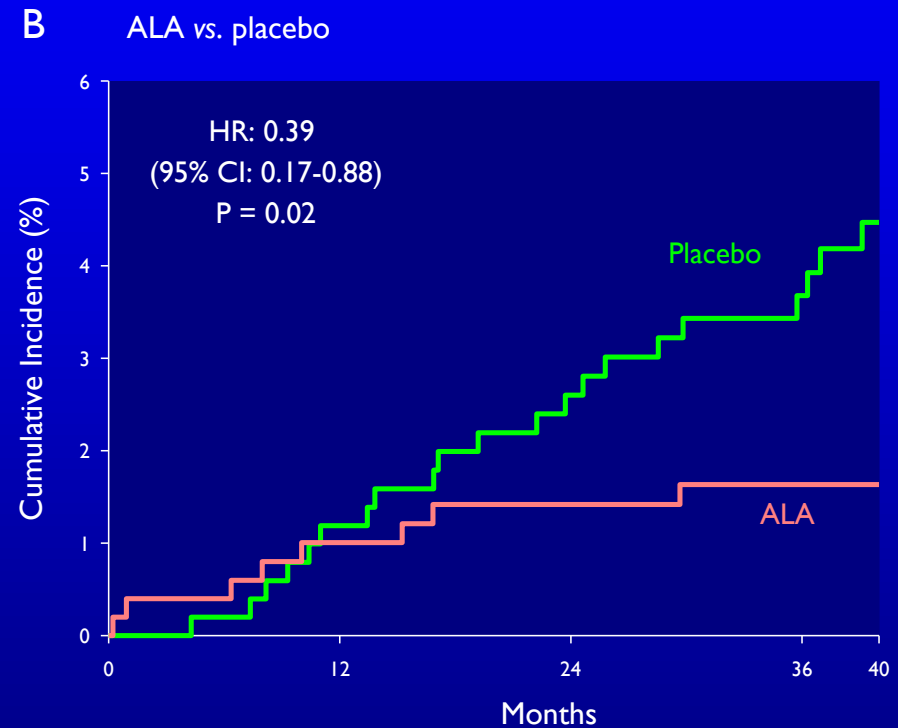
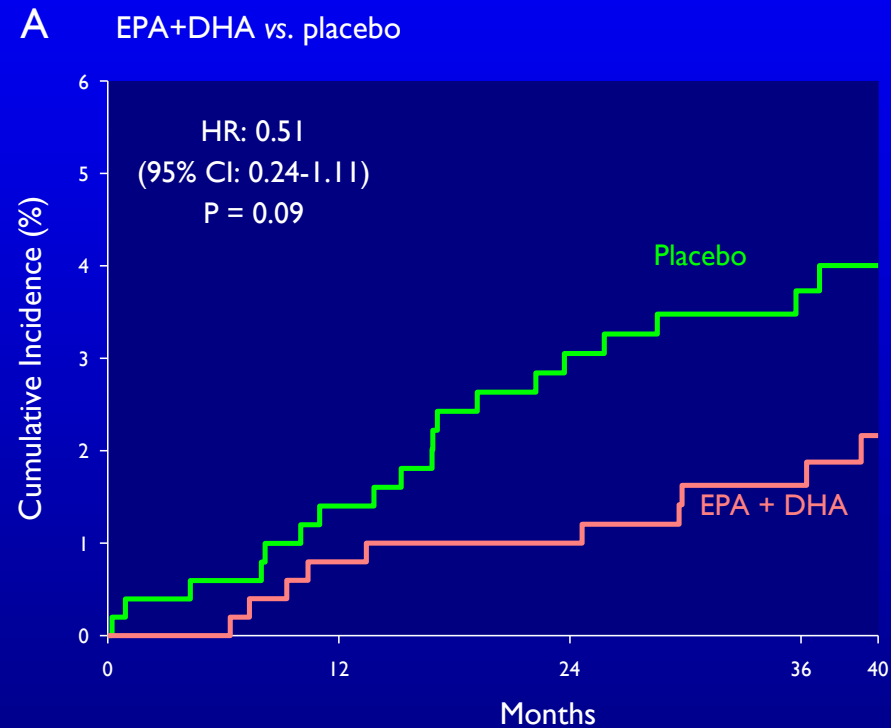
EPA+DHA better

Placebo better

ALA better

Placebo better

VENTRICULAR ARRHYTHMIA-RELATED EVENTS IN DIABETIC PATIENTS



Ventricular arrhythmia-related events:
defined as sudden death, cardiac arrest, and implantable cardioverter-defibrillator placement

CONCLUSIONS

- In the total patient population, low doses of n-3 fatty acids were not related to major cardiovascular events
- In **women**, ALA reduced major cardiovascular events borderline significantly
- In **diabetic patients**, n-3 fatty acids reduced ventricular arrhythmia-related events (exploratory analysis)

IMPLICATIONS

- Major cardiovascular events cannot be prevented by low doses of n-3 fatty acids in stable, well-treated post-MI patients
- ALA may prevent major cardiovascular events in women, which needs confirmation
- Whether n-3 fatty acids prevent ventricular arrhythmia-related events in post-MI patients with comorbid diabetes warrants further study