

ASCEND

A randomized trial of omega-3 fatty acids (fish oil) versus placebo for primary cardiovascular prevention in 15,480 patients with diabetes

Jane Armitage and Louise Bowman

on behalf of the ASCEND Study Collaborative Group

Funded by British Heart Foundation, UK Medical Research Council and support from Abbott, Bayer, Mylan and Solvay

Designed, conducted and analysed independently of the funders

University of Oxford is the trial sponsor



Declaration of interest

- Research contracts (Merck, The Medicines Company, Bayer, Mylan)

Background

- Diabetes increases cardiovascular risk, so a safe dietary supplement that reduced risk would be of value
- Higher fish intake is associated with lower cardiovascular risk
- Omega-3 (n-3) fatty acid (FA) supplements recommended for secondary prevention based on trials done in 1980s and 1990s
- Increased fish intake recommended for primary prevention
- Recent meta-analyses of randomized trials have not shown benefits of omega-3 fatty acids in primary or secondary prevention

ASCEND trial design

- Eligibility:** Age \geq 40 years; any DIABETES;
no prior cardiovascular disease
- Participants:** 15,480 UK patients
- Randomization:** Omega-3 fatty acids 1 g capsule/day vs placebo
(and aspirin 100 mg daily vs placebo)
- Follow-up:** Mean 7.4 years; >99% complete for morbidity & mortality
- Adherence:** Average adherence to omega-3 capsules 77%

Streamlined methods: mail-based (questionnaires & treatment); no study clinics; electronic health records; 2x2 factorial design; highly cost-effective

Baseline demographics (N=15,480)

Characteristic	Omega-3 FA	Placebo
Age, years	63	63
Male	63%	63%
Type 2 diabetes	94%	94%
Diabetes duration, median years	7	7
Hypertension	62%	62%
Statin use	75%	76%
Body Mass Index, kg/m ²	31	31
Glycated haemoglobin, mmol/mol	55 (7.2%)	55 (7.2%)

Key outcomes

Primary efficacy outcome: Serious Vascular Event (SVE)

Non-fatal myocardial infarction,

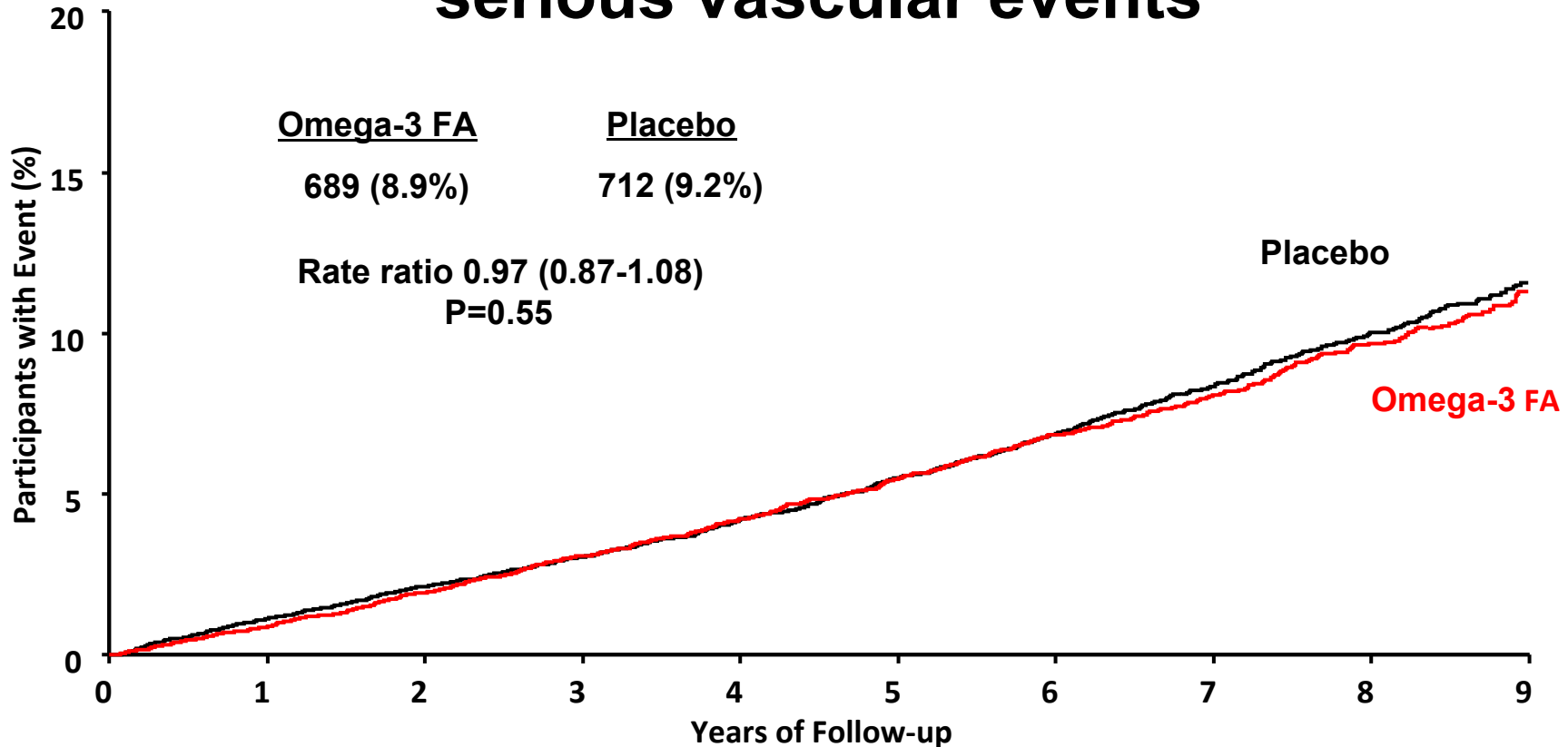
Non-haemorrhagic stroke or transient ischaemic attack, or

Cardiovascular death (excluding any intracranial haemorrhage)

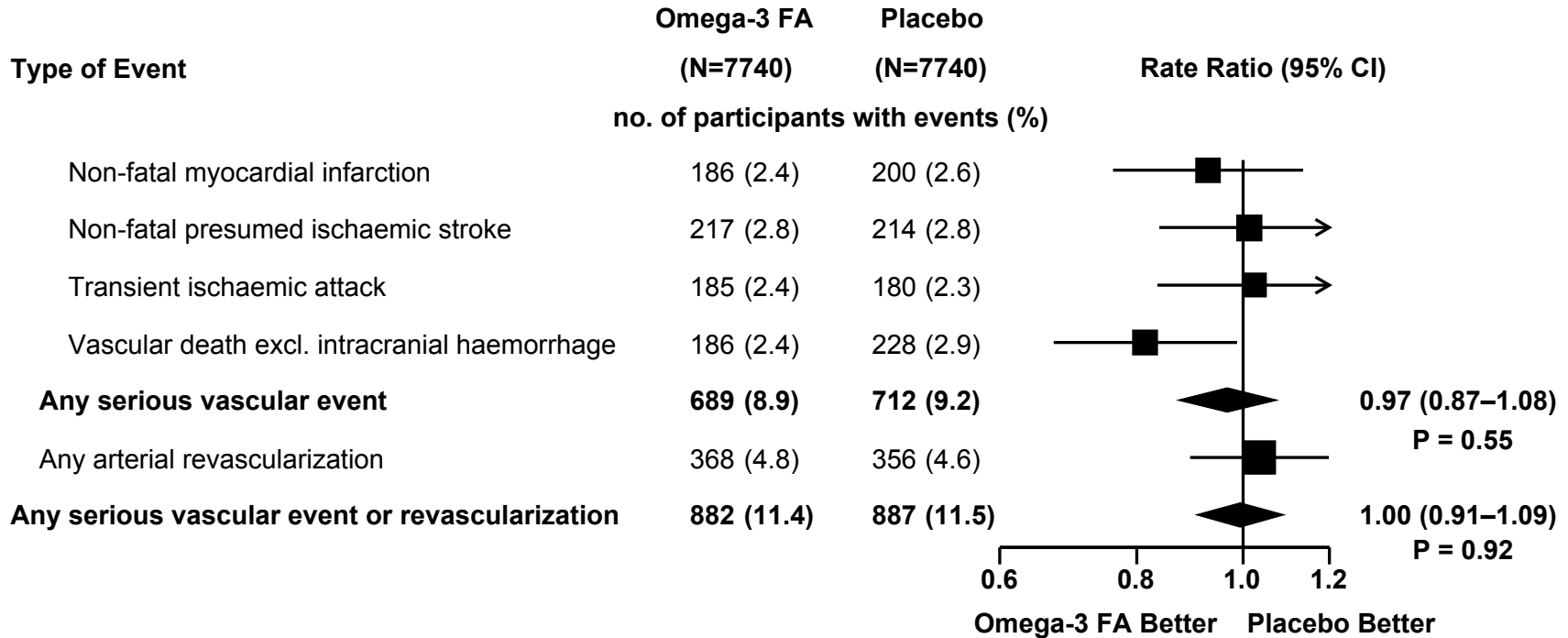
Secondary outcome: SVE or any revascularization

Pre-specified for subgroup analyses

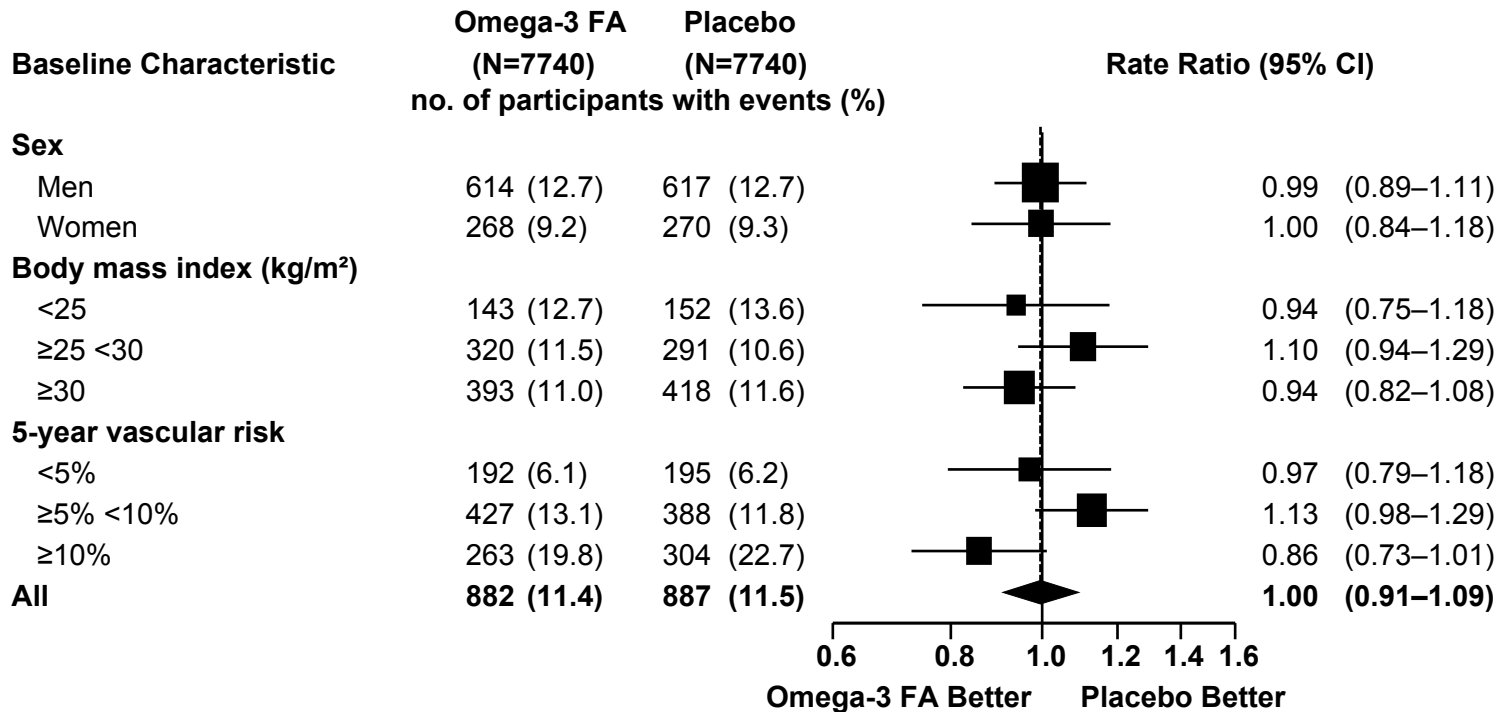
Effect of omega-3 FA supplements on serious vascular events



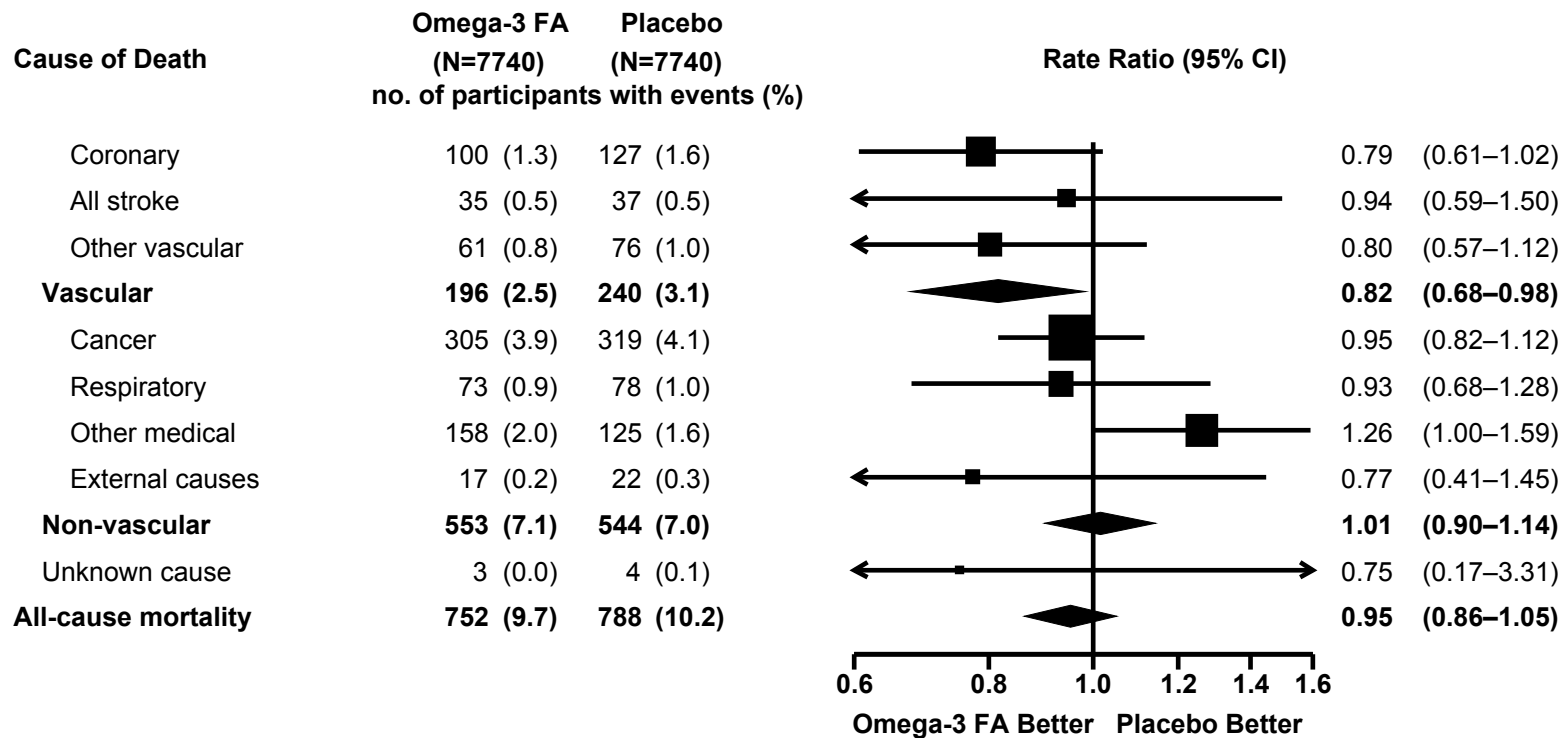
Effect of omega-3 FA supplements on vascular events



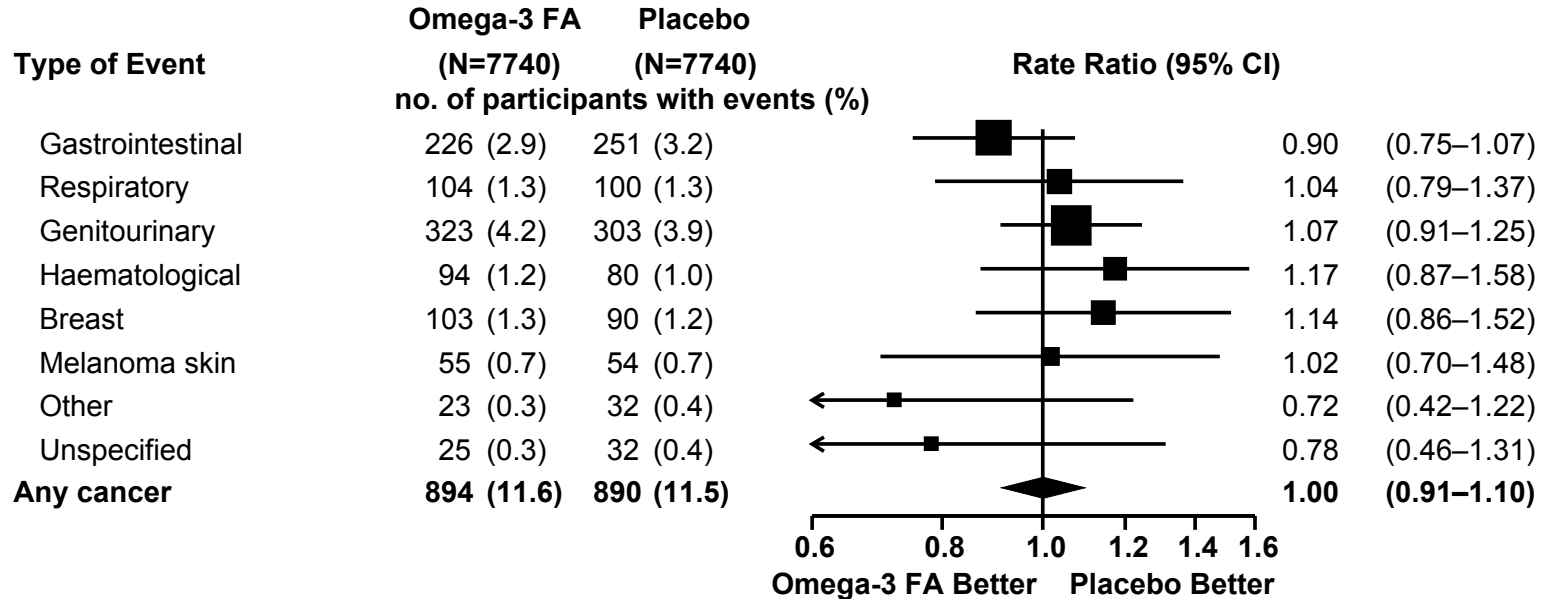
Effects of omega-3 FA supplements on SVE or revascularization in different types of participant



Effect of omega-3 FA supplements on cause-specific mortality



Effect of omega-3 FA supplements on site-specific cancer



Fish oil supplements are widely used

- Estimated global market for omega-3 products was \$31 billion in 2015
- In a large UK prospective study, 31% of adults reported taking fish oils
- Estimates suggest 19 million people in the US take fish oil supplements
- Benefits claimed on: heart, brain, weight, vision, inflammation, skin, pregnancy, liver fat, depression, childhood behaviour, mental decline, allergies, bones...
- Environmental costs debated



Summary: Omega-3 FA supplementation in diabetes

- ASCEND is the largest and longest duration placebo-controlled randomized trial of omega-3 FA supplementation
- No effect on primary outcome of serious vascular events
- No effect on cancer, total or cause-specific mortality
- No safety concerns

Guideline recommendations should be reconsidered



The NEW ENGLAND
JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of n-3 Fatty Acid Supplements in Diabetes Mellitus

The ASCEND Study Collaborative Group*