

ASCEND

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

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on behalf of the ASCEND Study Collaborative Group

Funded by British Heart Foundation, UK Medical Research Council
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Designed, conducted and analysed independently of the funders
University of Oxford is the trial sponsor



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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

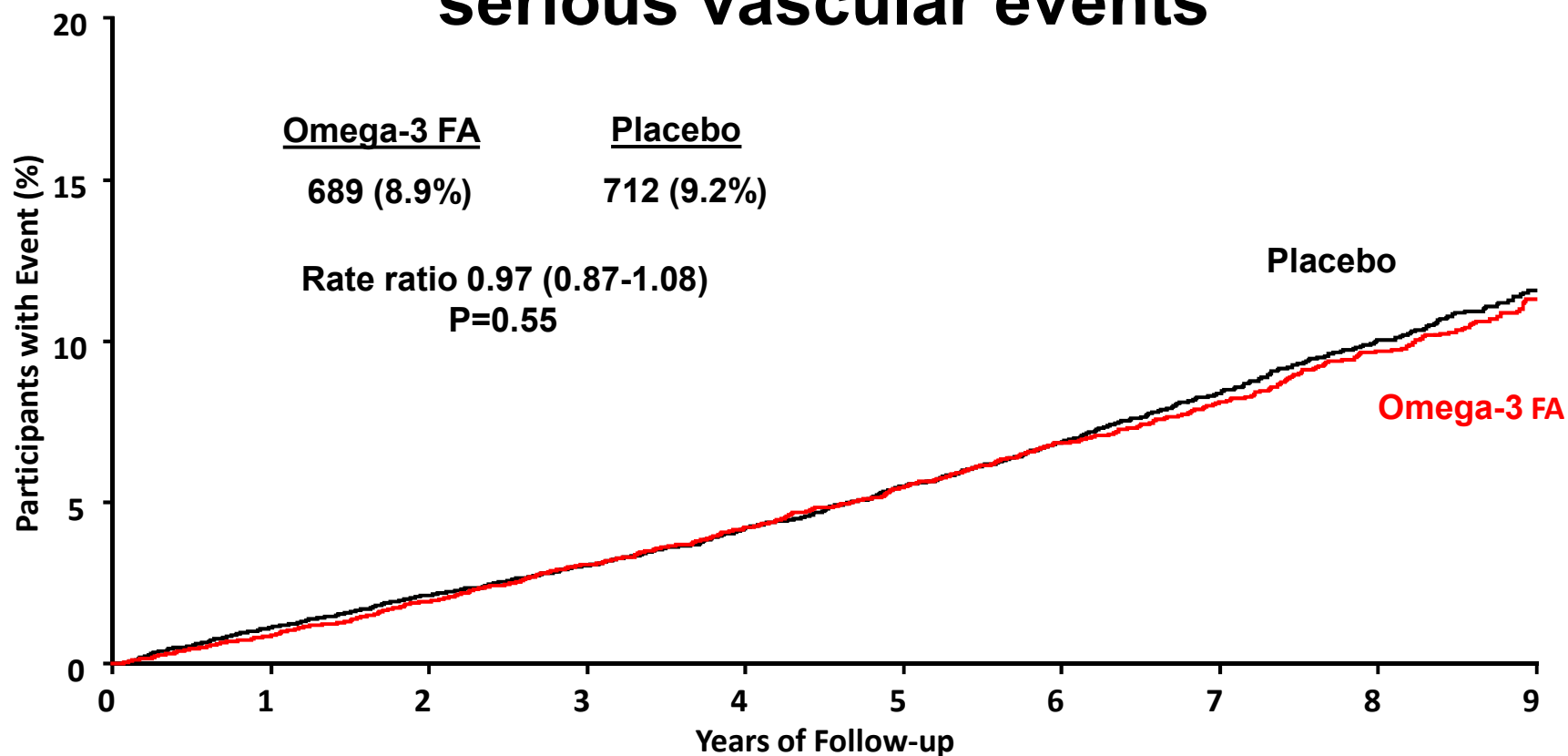
Primary efficacy outcome: Serious Vascular Event (SVE)

Non-fatal myocardial infarction,
Non-haemorrhagic stroke or transient ischaemic attack, or
Cardiovascular death (excluding any intracranial haemorrhage)

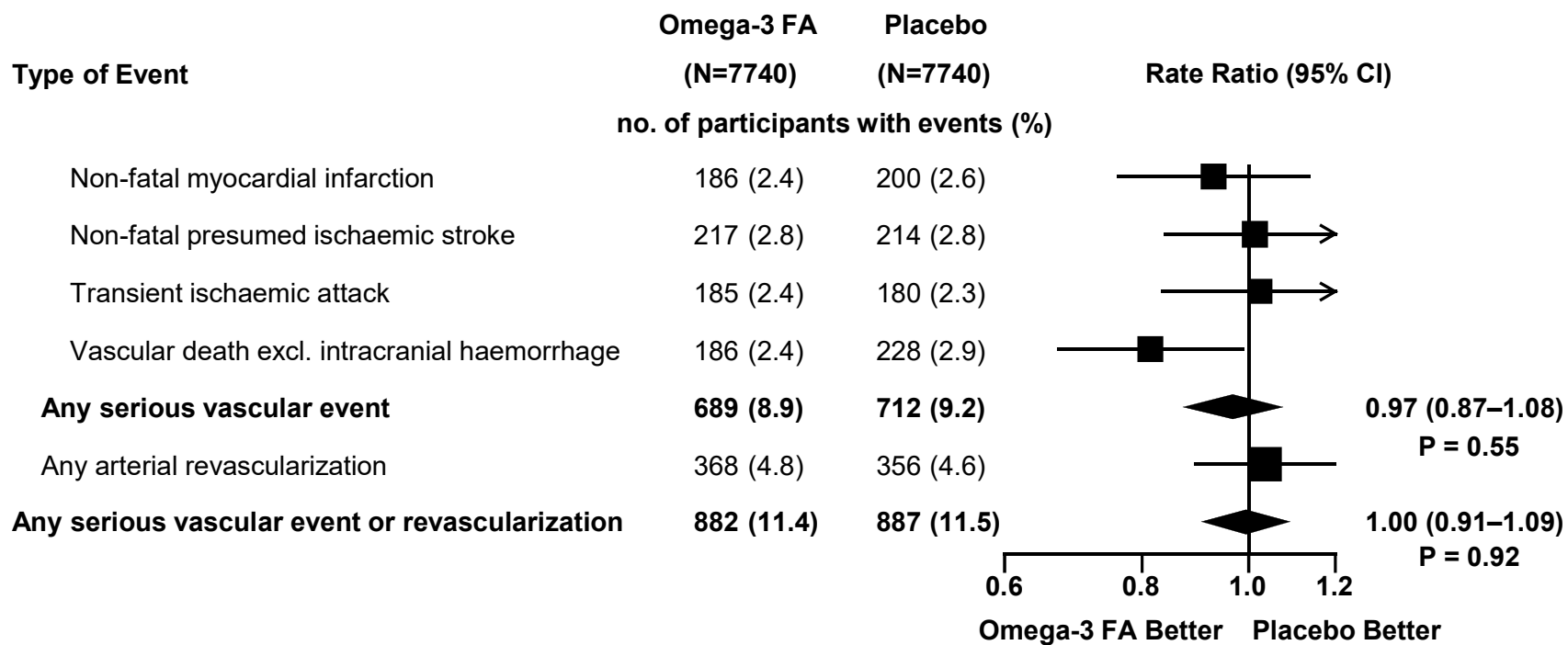
Secondary outcome: SVE or any revascularization

Pre-specified for subgroup analyses

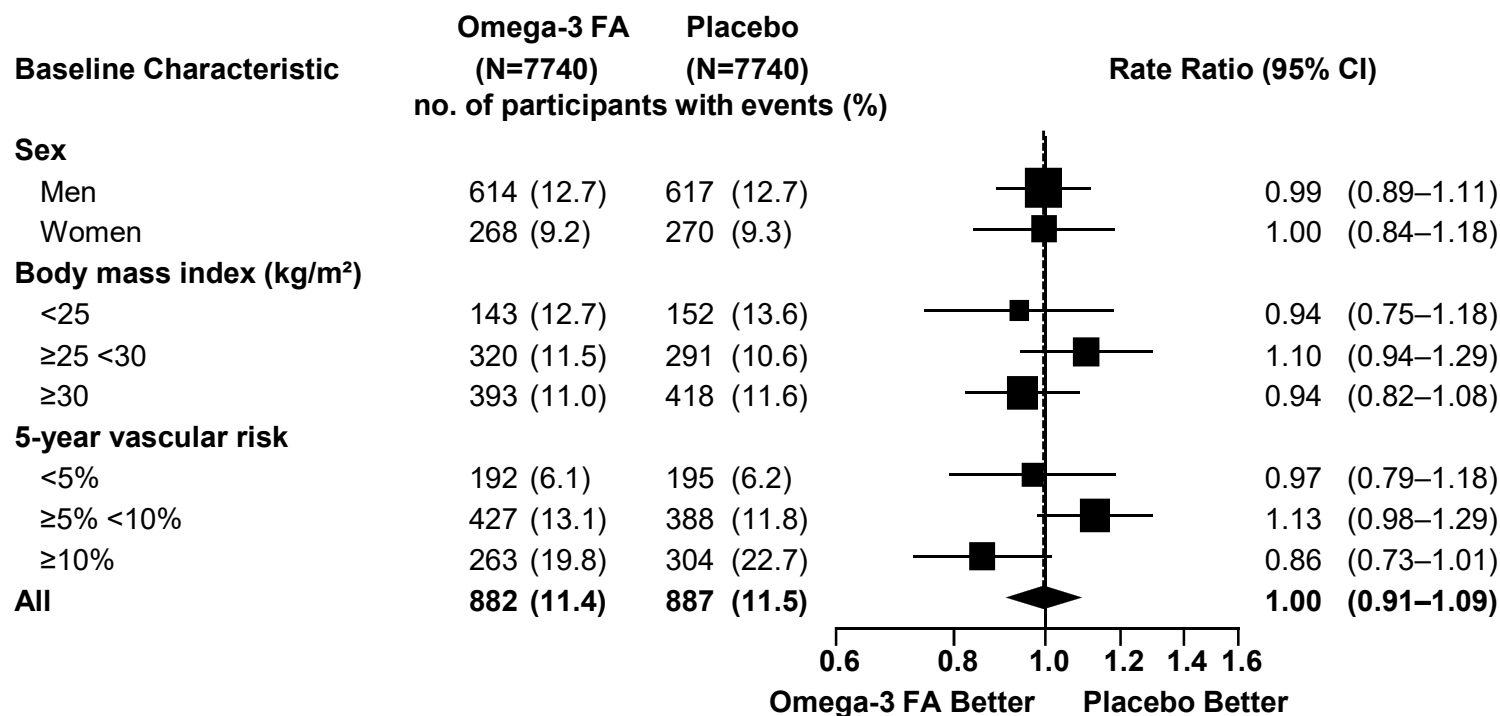
Effect of omega-3 FA supplements on serious vascular events



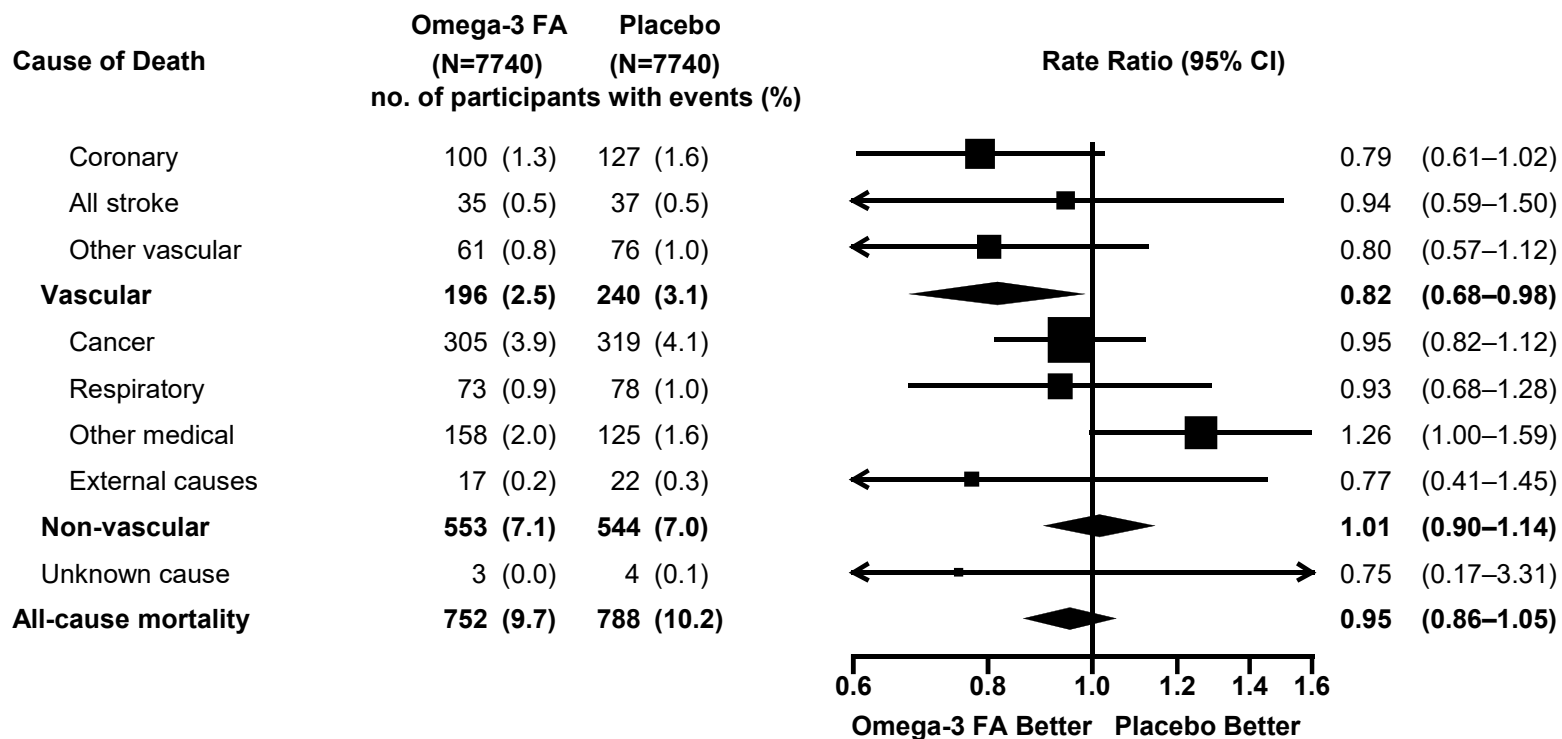
Effect of omega-3 FA supplements on vascular events



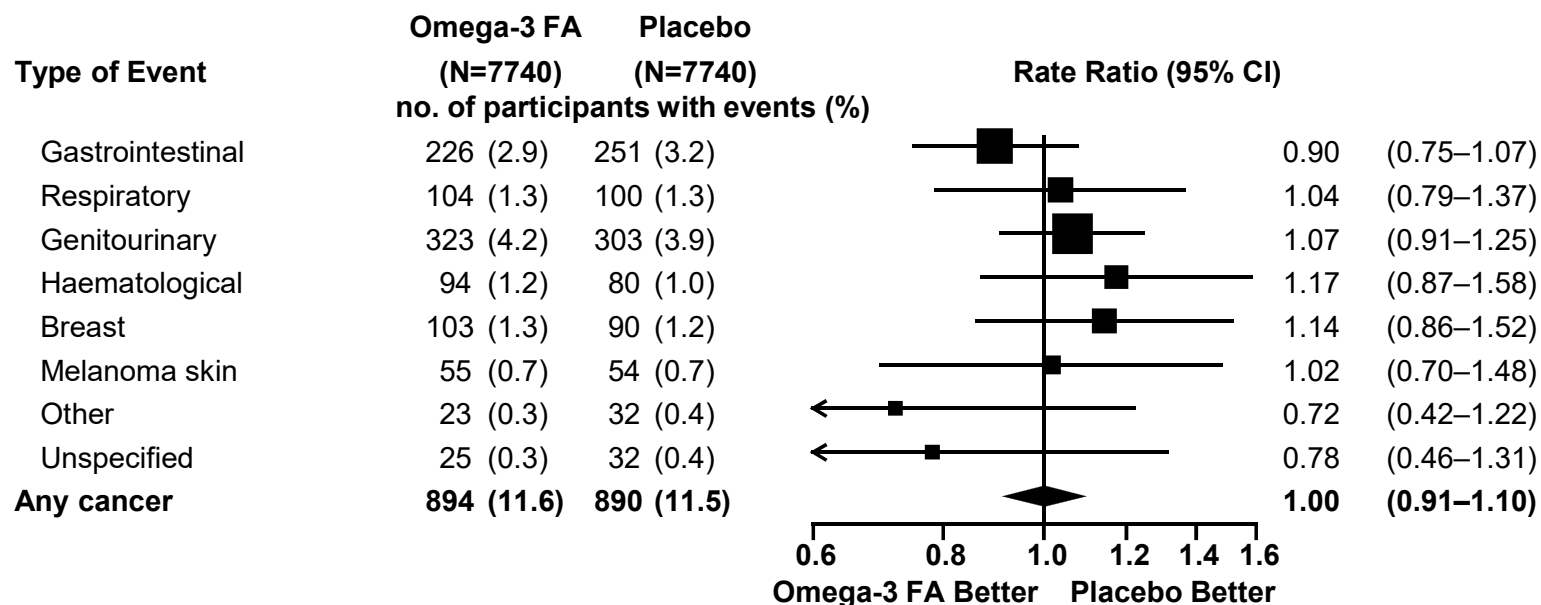
Effects of omega-3 FA supplements on SVE or revascularization in different types of participant



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
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ORIGINAL ARTICLE

Effects of n–3 Fatty Acid Supplements in Diabetes Mellitus

The ASCEND Study Collaborative Group*