Effects of omega−3 fatty acid supplements on arrhythmias in ASCEND

Sarah Parish and Jane Armitage
on behalf of the ASCEND Study Collaborative Group

ESC Congress Paris 2019
Together with World Congress of Cardiology

Declaration of interest

- Research contracts (Grants to the University of Oxford from the British Heart Foundation, the UK Medical Research Council and Cancer Research UK)
- Others (ASCEND study drugs were provided by Solvay, Abbott, Mylan and Baye

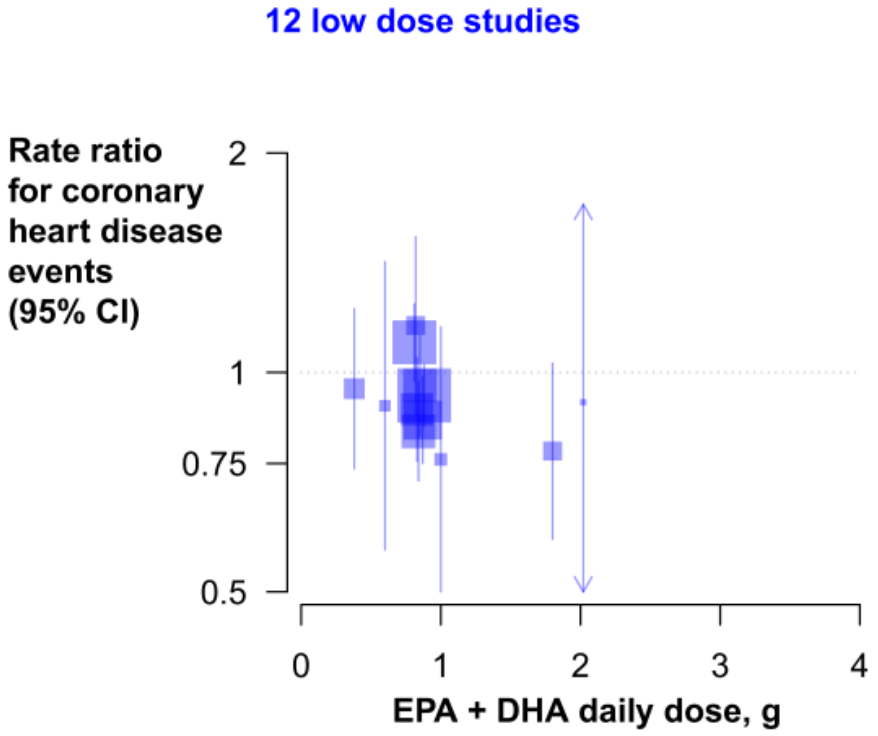
Background

- Higher fish consumption is associated with lower risks of coronary heart disease, and particularly of cardiac deaths, in observational studies

- 2018 meta-analyses of randomized trials of 0.5-2 g daily omega-3 fatty acid supplementation (EPA+DHA) did not show convincing benefit on CVD

- Three further large trials have since reported

Omega-3 fatty acid supplementation and coronary events in randomized trials



Aung, JAMA Cardiol 2018; ASCEND, NEJM 2018; Manson, NEJM 2019; Bhatt, NEJM 2019

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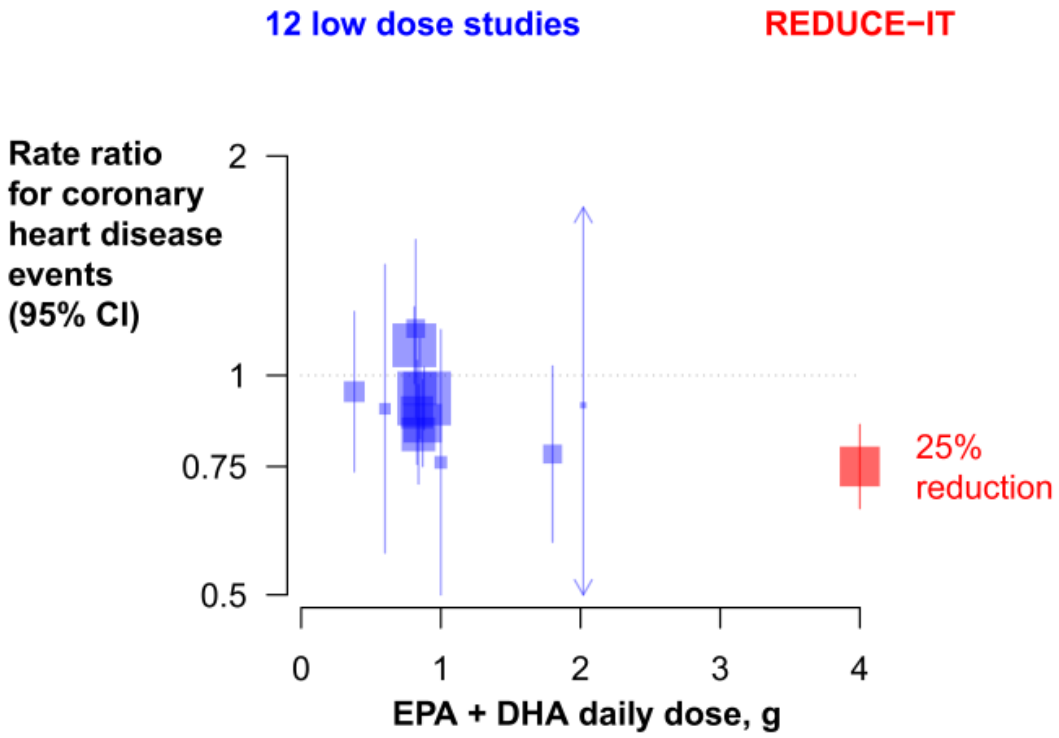

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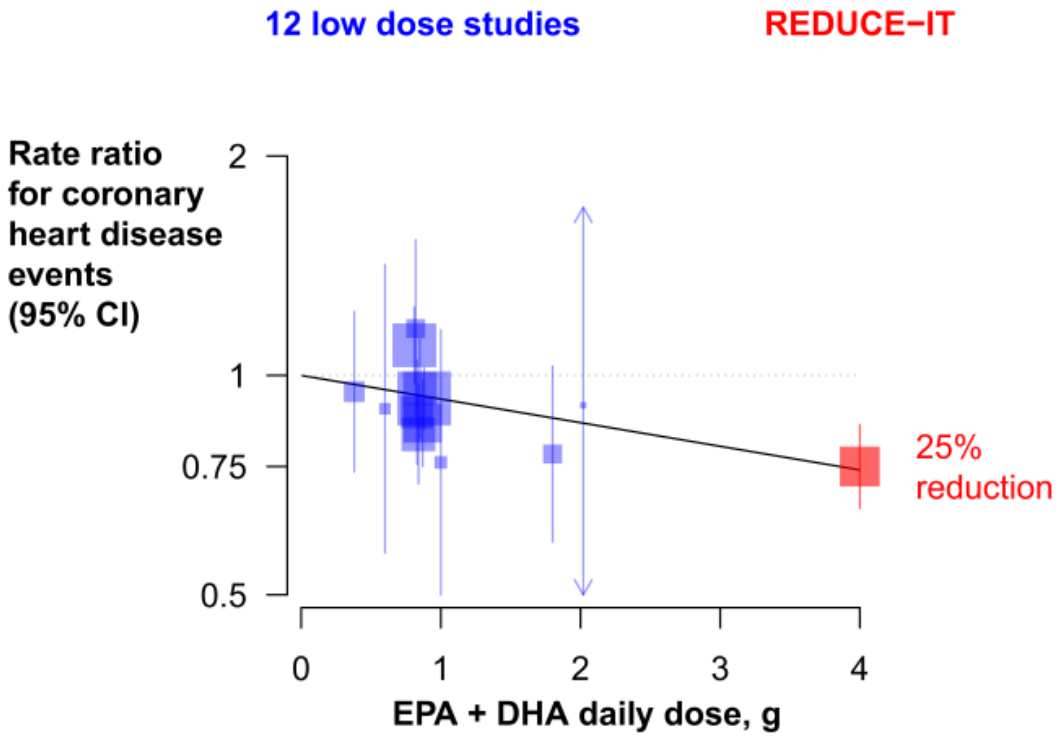

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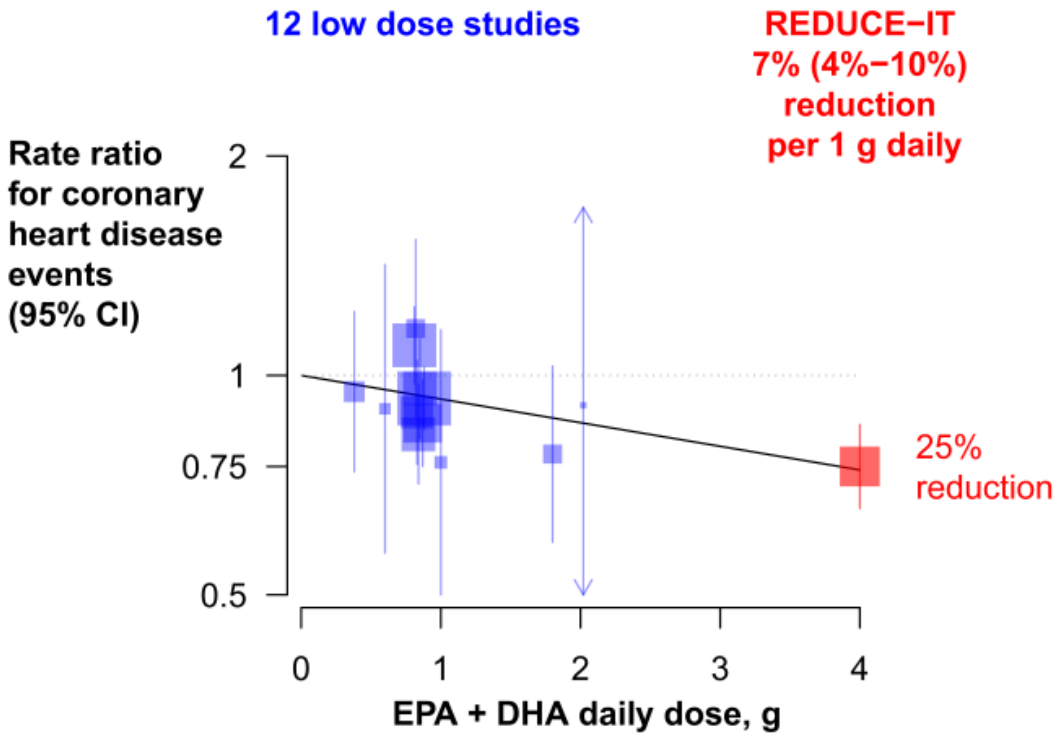

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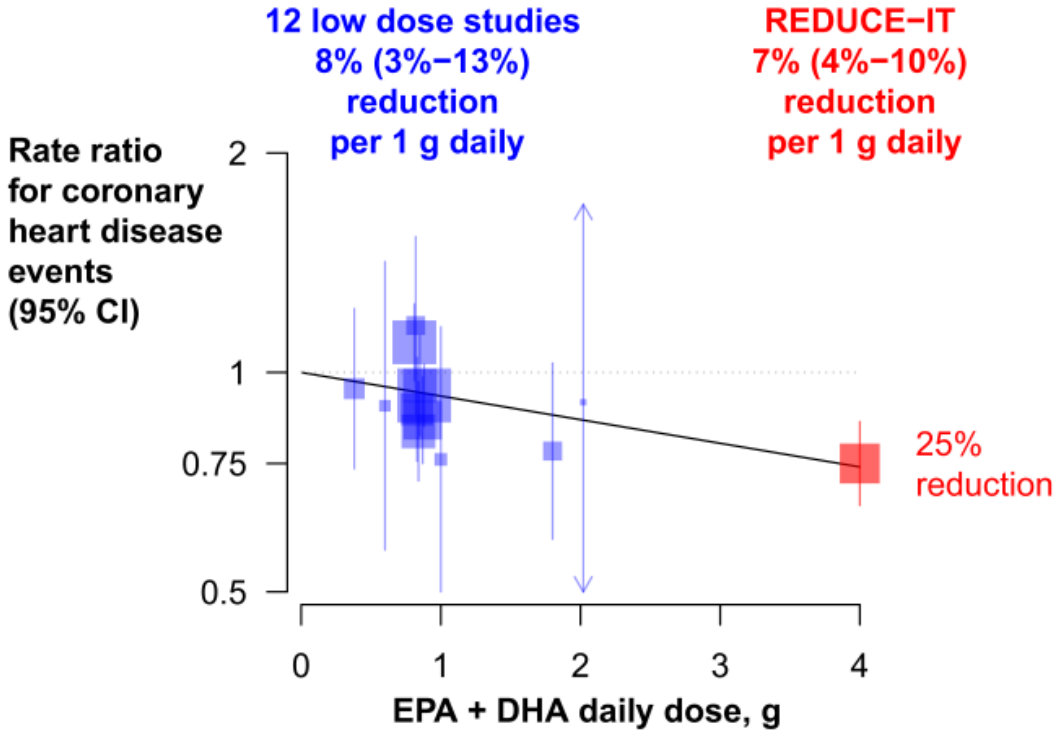

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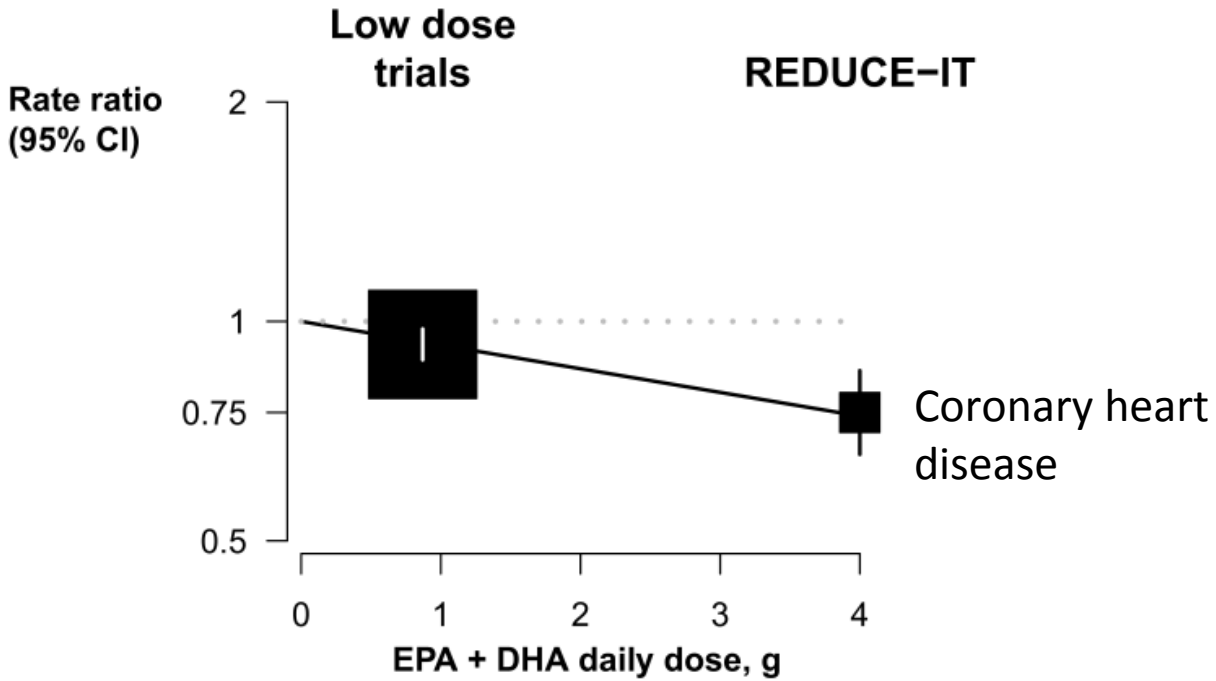
Omega-3 fatty acid supplementation: outcomes in REDUCE-IT



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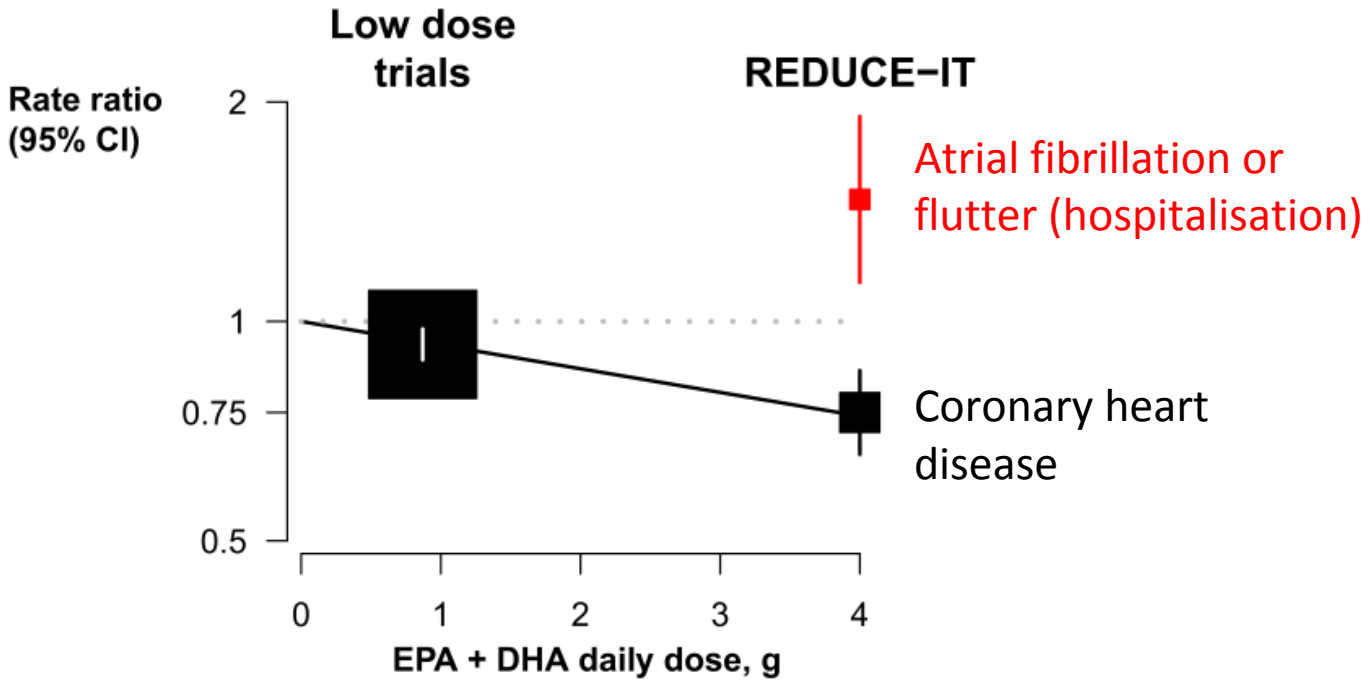

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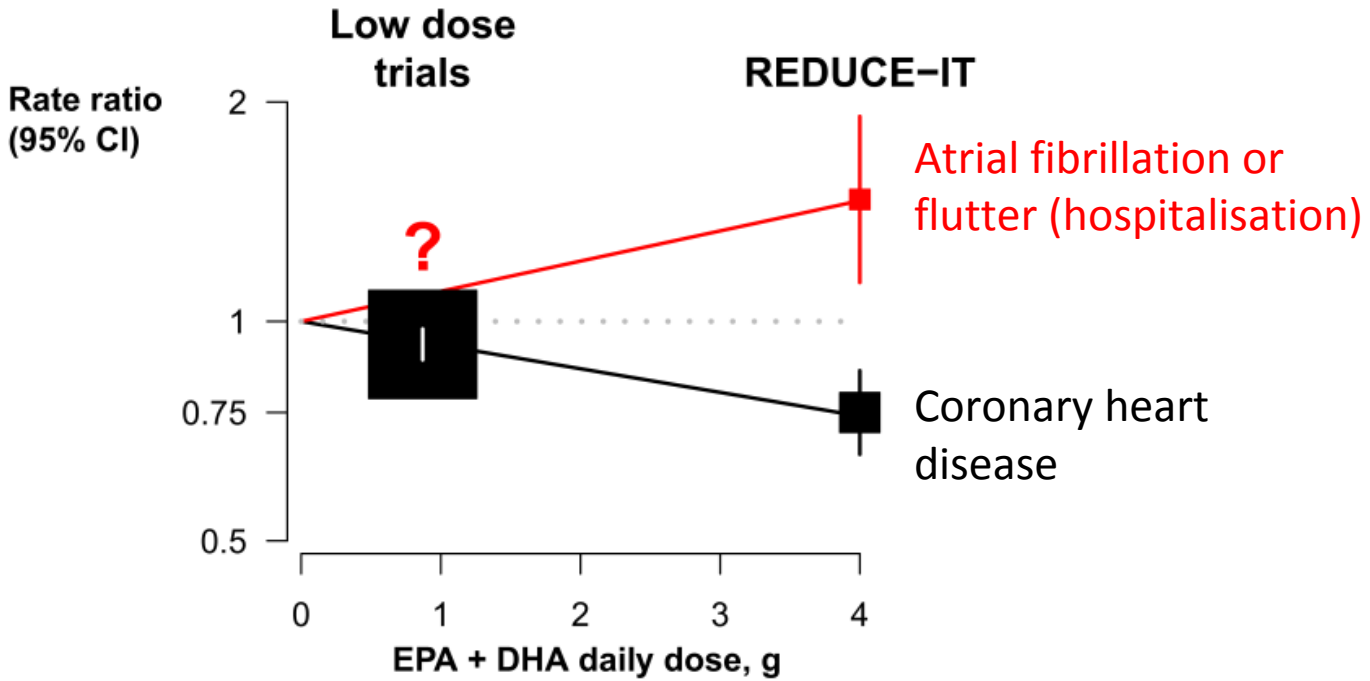

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ASCEND trial design

Eligibility:	Age ≥ 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)
Exclusion:	Current anticoagulation use
Follow-up:	Mean 7.4 years; >99% complete for morbidity & mortality
	97% with linkage to electronic Hospital Episode Statistics data during trial (and for 14 years before randomization)
Adherence:	Average adherence to omega-3 capsules 77%

ASCEND Study Collaborative Group: Trials 2016 / Am Heart J 2018/ NEJM 2018

Arrhythmia outcomes

Arrhythmia outcomes defined from:

- Hospitalisations or serious events reported by participants during the trial
- ICD10-code diagnoses and OPCS4 procedure codes in electronic Hospital Episode Statistics data

Key outcomes considered:

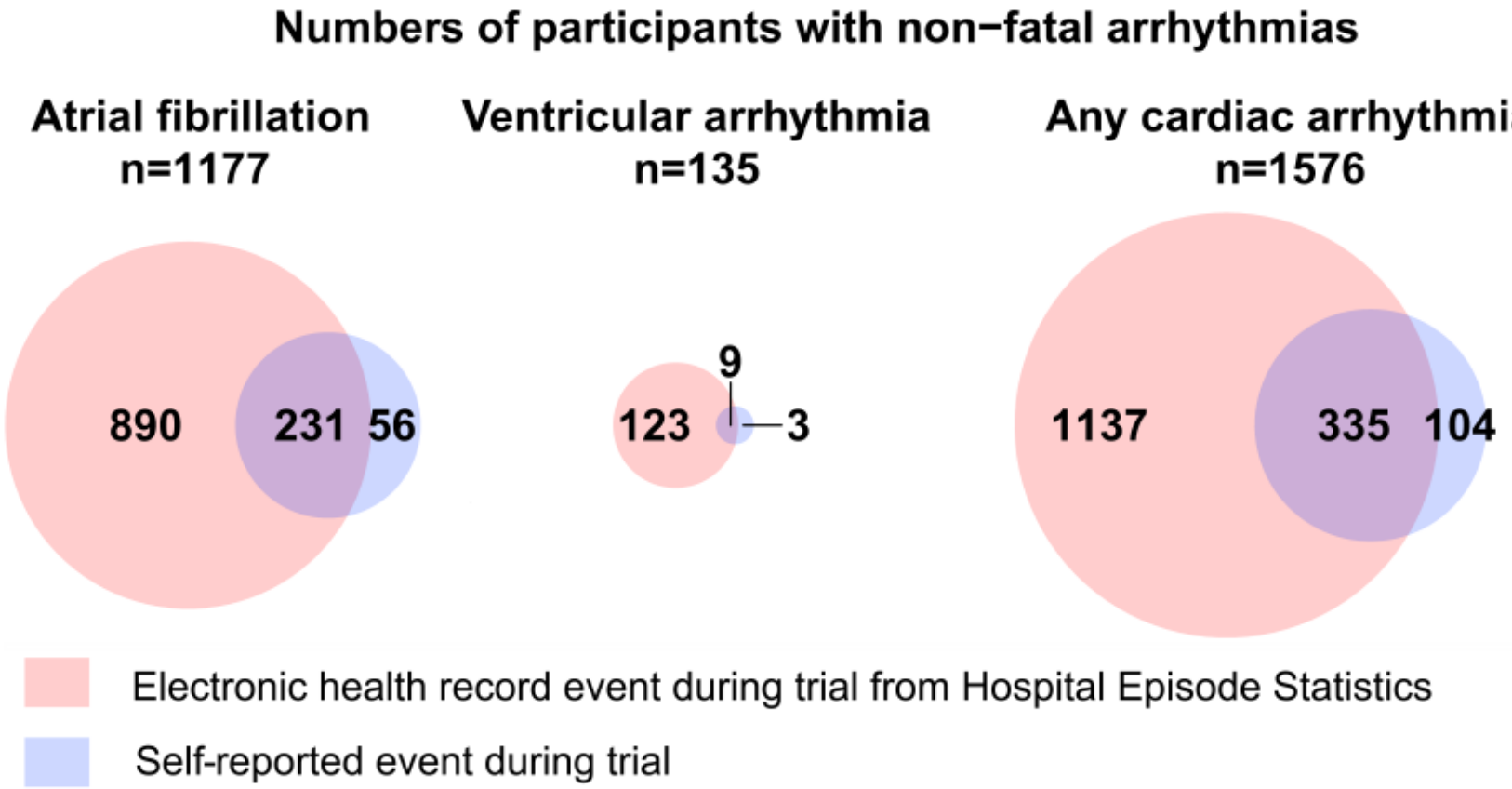
- Atrial fibrillation (AF) in participants without known prior AF
- Non-fatal ventricular arrhythmia
- Any non-fatal cardiac arrhythmia

  (AF, bradyarrhythmia, ventricular or supraventricular arrhythmia)
- Cardiac death

Baseline demographics (N=15,480)

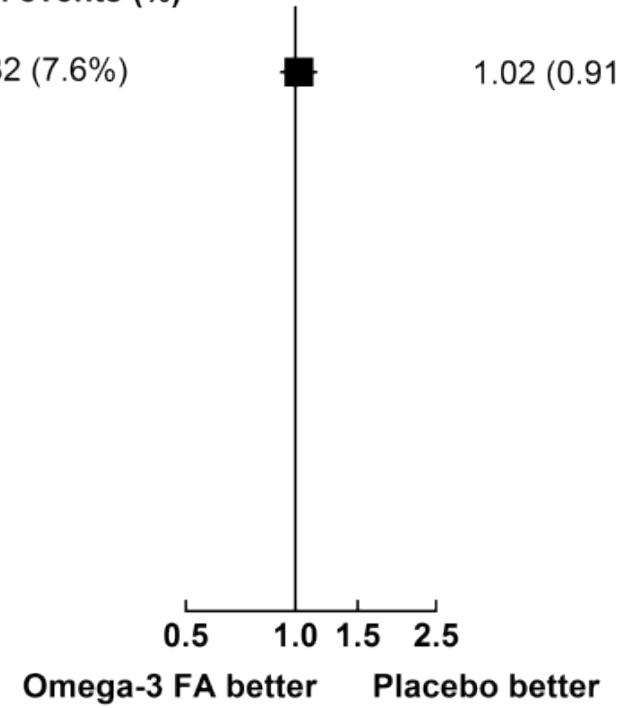
Characteristic	Omega-3 FA	Placebo
Age, years	63	63
Male	63%	63%
Hypertension	62%	62%
Statin use	75%	76%
Body Mass Index, kg/m^2	31	31
Prior admission with atrial fibrillation	0.7%	0.6%

Arrhythmia outcomes from self-report vs EHR



Effect of omega-3 FA supplements on arrhythmias and cardiac deaths

Non-fatal arrhythmias	Omega-3 FA (N=7740) N participants with events (%)	Placebo (N=7740)	Rate ratio (95% CI)
Atrial fibrillation (AF)	595 (7.7%)	582 (7.6%)	1.02 (0.91, 1.15)



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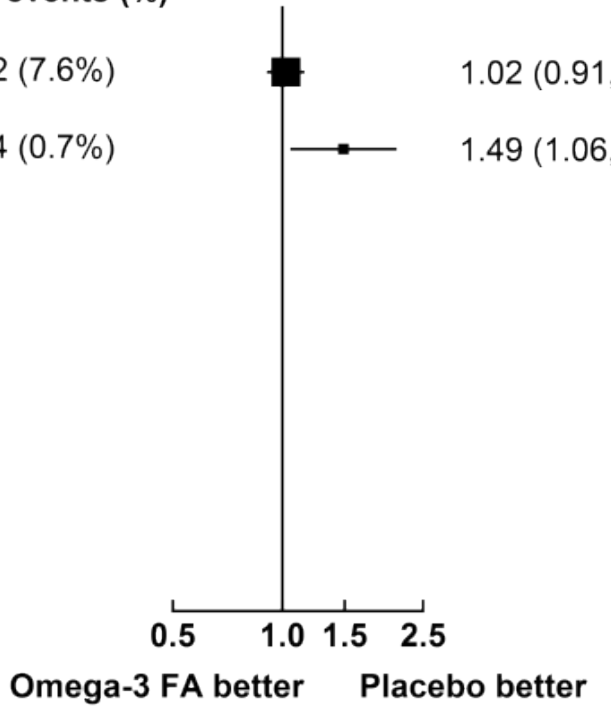

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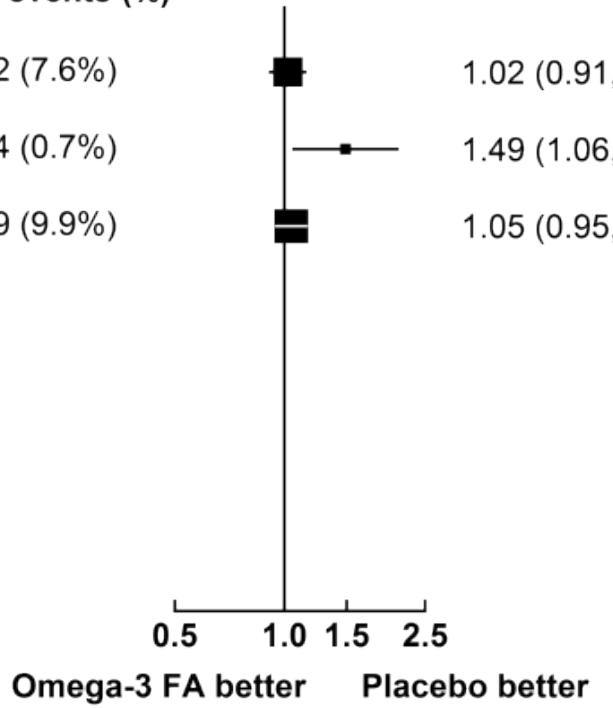

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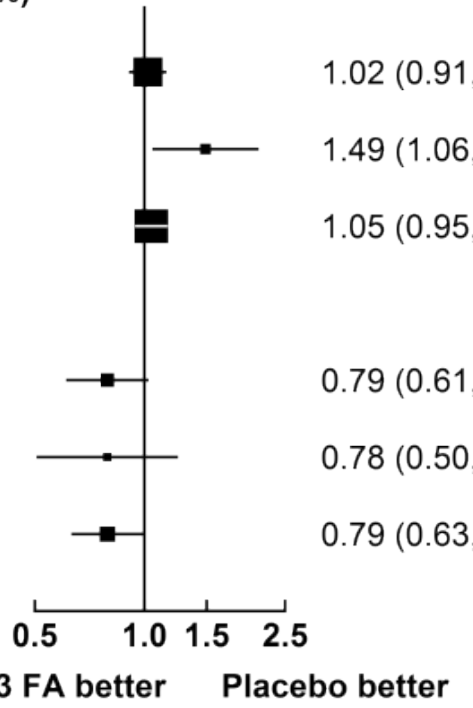
Cardiac deaths			
Coronary death	100 (1.3%)	127 (1.6%)	0.79 (0.61, 1.02)
Non-coronary cardiac death	33 (0.4%)	42 (0.5%)	0.78 (0.50, 1.23)
Any cardiac death	133 (1.7%)	169 (2.2%)	0.79 (0.63, 0.98)



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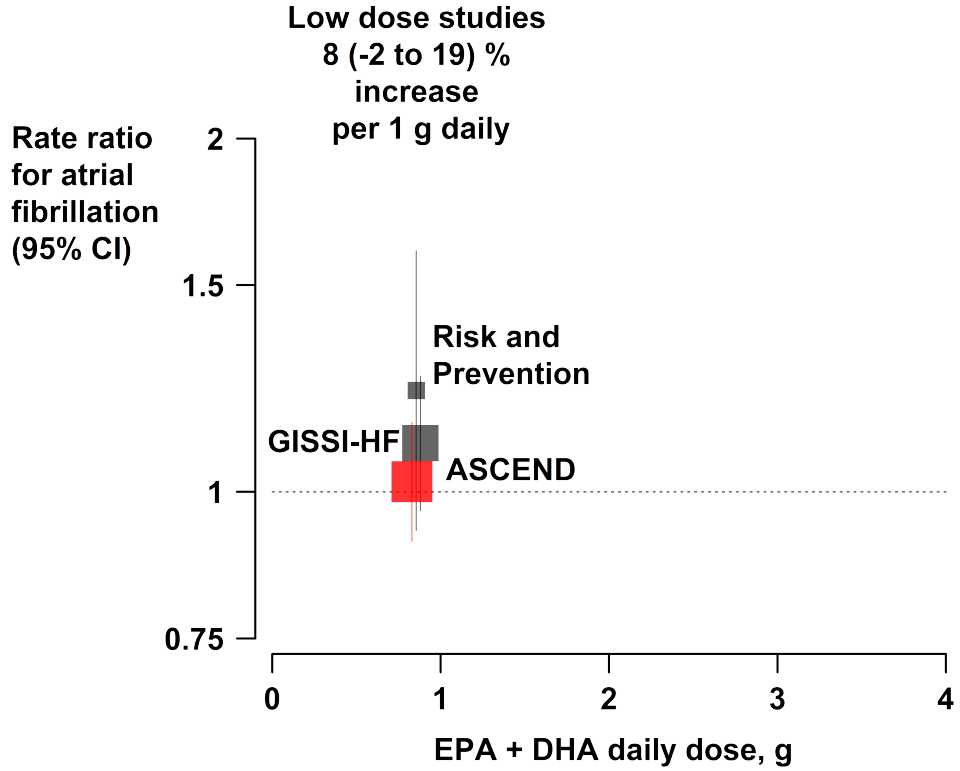

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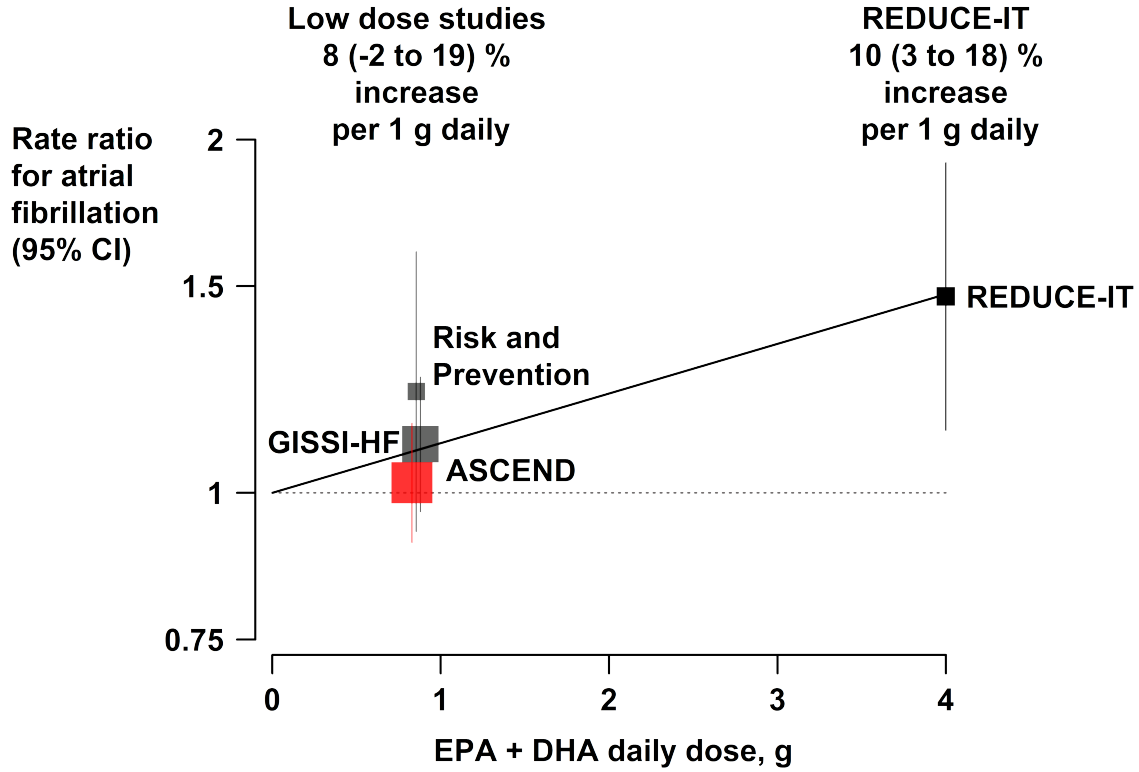

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Summary: arrhythmias in ASCEND

- ASCEND provides randomized evidence of the effects of 1 g daily omega -3 FA capsules on arrhythmias
- No statistically significantly effect on atrial fibrillation
- No statistically significantly effect on any non-fatal cardiac arrhythmia

Conclusions

- Evidence from 13 large trials suggests that omega-3 FA supplementation may have a dose-related protective effect on coronary events
- May also be a dose-related adverse effect on non-fatal arrhythmias
- Systematic reporting of arrhythmia outcomes in existing and future trials is required
- The ongoing STRENGTH trial using 4 g daily supplementation will be able to add importantly when it completes next year