

**ALPHA OMEGA: Effect of low doses of
n-3 fatty acids on cardiovascular diseases in
post-MI patients.
Editorial Comment**

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Discussant

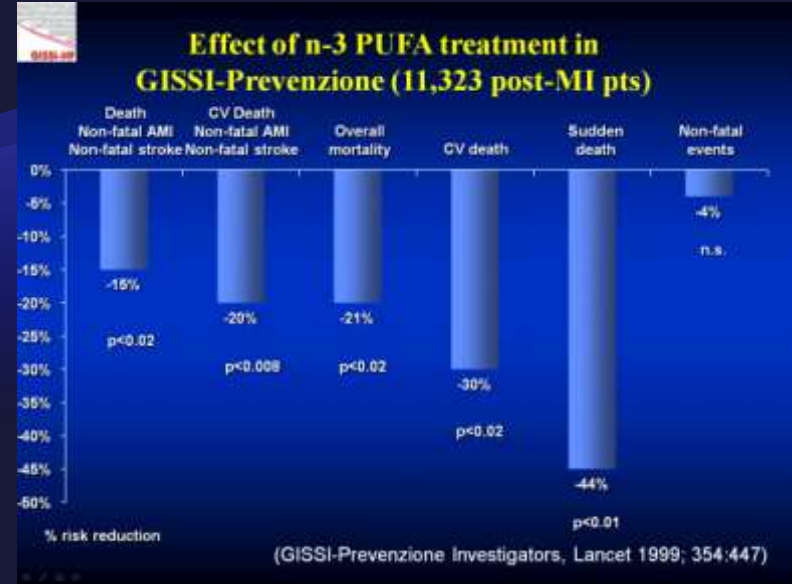
DART

DART: Results (3)

Survival: Fish Advice

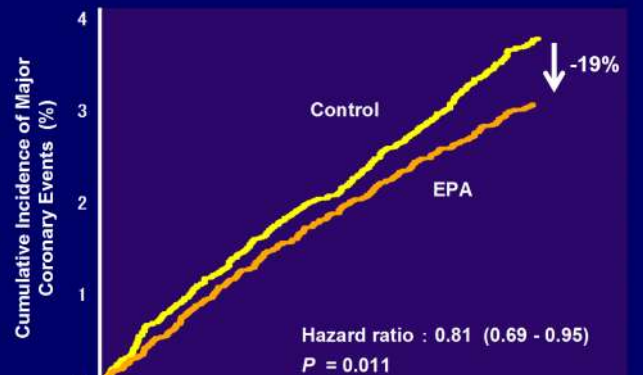


GISSI-Prevenzione



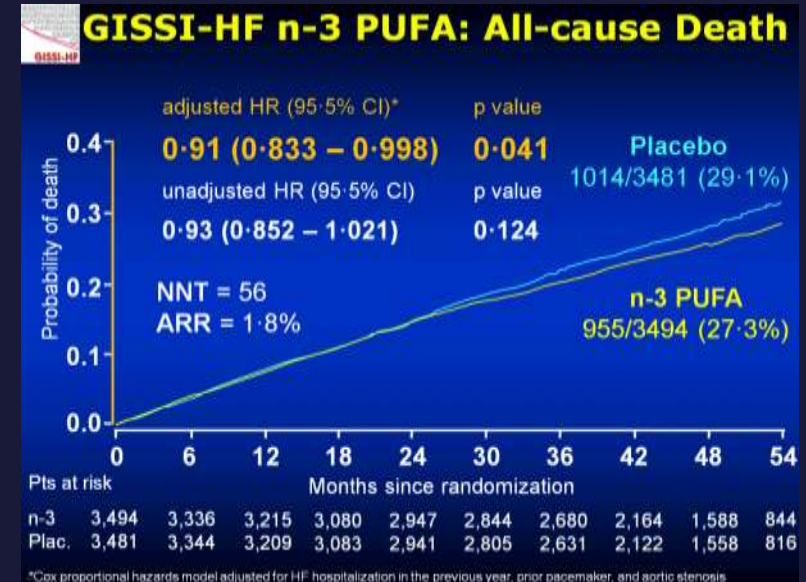
JELIS

Kaplan-Meier estimates of major coronary events



No at Risk	0	1	2	3	4	5
Control	9,319	8,931	8,671	8,433	8,192	7,958
EPA	9,326	8,929	8,658	8,389	8,153	7,924

GISSI-HF



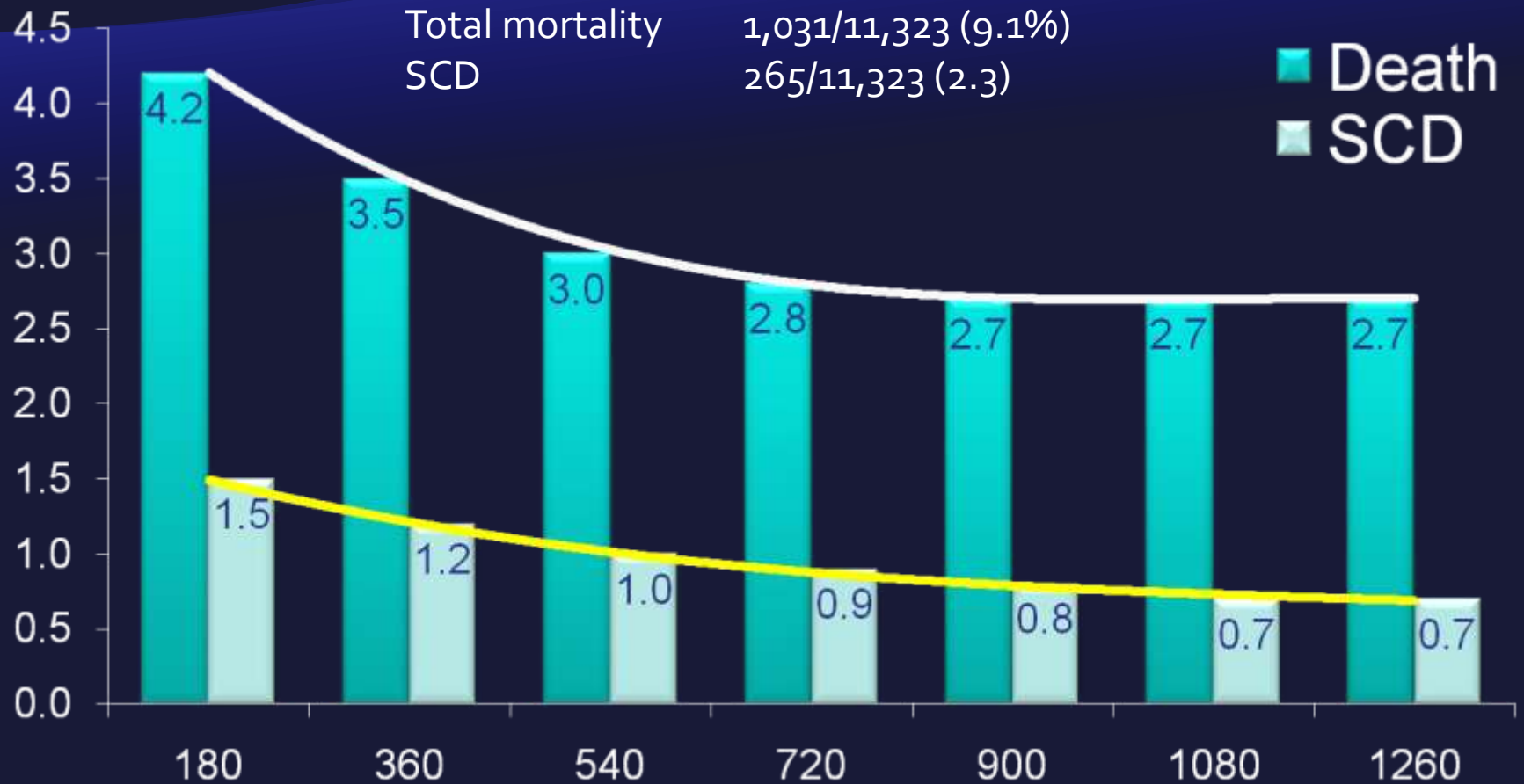
Why neutral results?

- ◆ Was the hypothesis sound enough?
- ◆ Low n-3 PUFA dose?
- ◆ How large is large enough?
- ◆ Optimistic expectations of benefit ?
- ◆ Were the components of the composite primary endpoint specific enough for the specific mechanisms of action of n-3 PUFA?
- ◆ Too pragmatic study conduct ?

Assumptions

- ◆ incidence of **CHD mortality of 4% per year** in patients aged 60 to 80, enrolled 3.7 years (median) after MI
- ◆ 25% risk of CHD mortality reduction for EPA+DHA and 20% for ALA over 3 years (2 ways analysis)

GISSI-Prevenzione trial (1999)

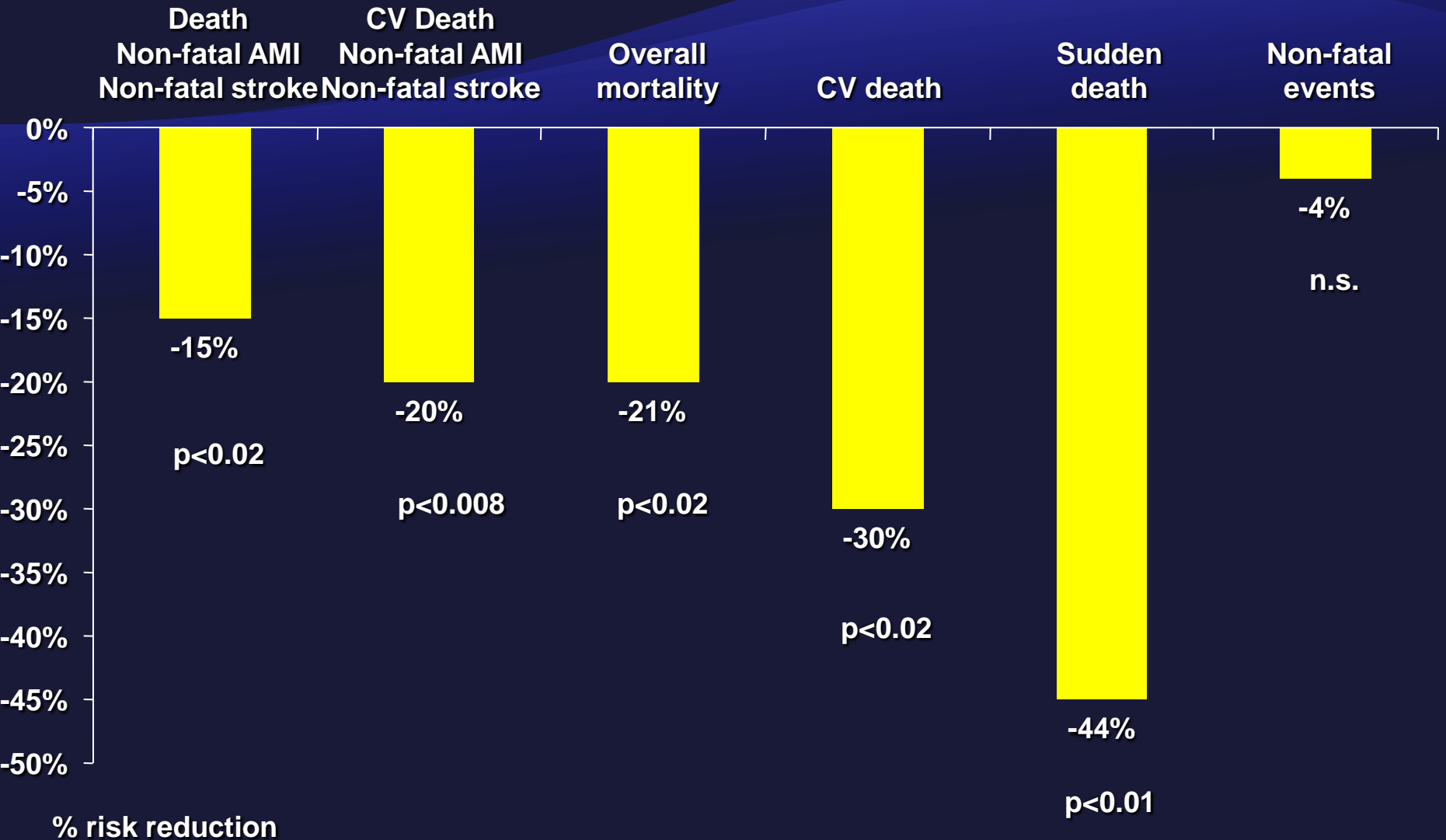


- ◆ During the course of the study the Steering Committee approved an increase in sample size from 4,000 to 4,837 subjects and an extended duration of intervention from 36 to 40 months.
- ◆ In 2009 the original primary endpoint of “fatal CHD” was replaced by “major CV events” (including all fatal/non-fatal CV events and therapeutic interventions)

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Effect of n-3 PUFA treatment in GISSI-Prevenzione (11.323 post-MI pts)



(GISSI-Prevenzione Investigators, Lancet 1999; 354:447)

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Methods

- ◆ Subjects were identified by hospital cardiologists, physically examined at enrollment by trained research nurses, and followed up by research staff through telephone interviews at 12 and 24 months (only)
- ◆ **Non-fatal** cardiovascular events were **self-reported** and verified (*if known*) against hospital records (*if available*), otherwise they were not considered

Conclusions

- ◆ The AOT Investigators are to be praised for this independent, investigator-initiated, **food-based**, randomized, placebo controlled trial which was conducted with limited governmental funds.
- ◆ The pragmatic approach, the low dose of EPA+DHA, and the small sample size do not allow to draw firm conclusions about the effect of n-3 PUFA in this population.

END