

**NORVIT: Randomized trial of
homocysteine lowering with B-vitamins
for secondary prevention of
cardiovascular disease after acute
myocardial infarction**

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NORVIT- Discussion 1

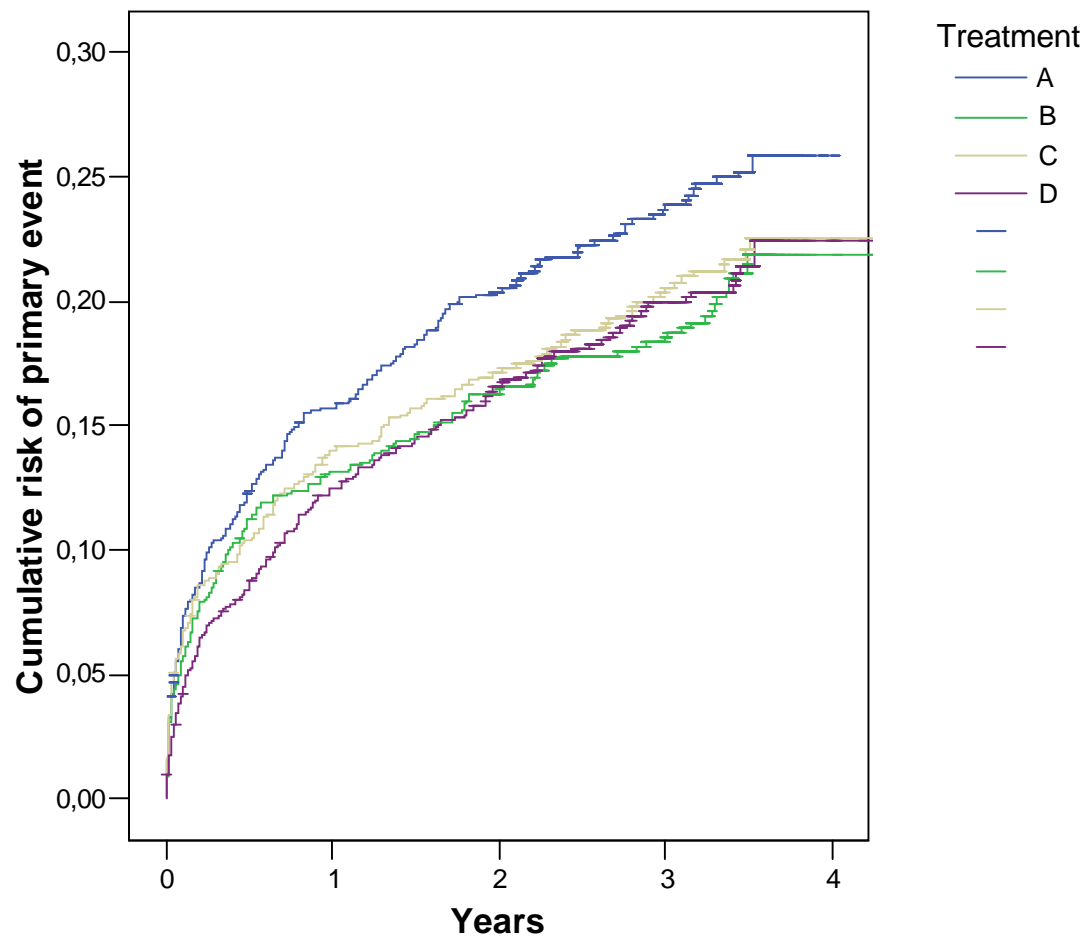
- Randomized control secondary prevention trial, factorial design: FA+B12+B6; FA+B12; B6; Placebo
- N=3749. 716 end-points over 3.5 years
- Design, execution and analysis appeared independent of any vested interests
- Groups well matched
- 90% on ASA and beta blockers; 80% on statins; 30% on ACE inhibitors
- 30% on vitamin supplements at baseline
- Baseline Hcy \geq 13 $\mu\text{mol/L}$ associated with 27% increased risk in all groups
- No identifiable benefit from use of B vitamins despite a 25% reduction in Hcy with FA and B12 but not B6

NORVIT- Discussion 2

	FA,B12,B6	FA,B12	B6	Placebo
No:	937	935	934	943
MI+CVA	210	168	175	172
MI	182	147	161	153
All deaths	104	80	92	89
Cancer	33	33	22	25

The NORVIT trial

Risk of primary event by treatment group



P=0.029 for A vs B-D

NORVIT Discussion 3

- Was the study adequately powered? Perhaps not
- Clever factorial design, but was it too complex? Cannot isolate the effect of folate, but it was a trial of Hcy lowering, not of folate per se
- Comparison with the powerful effects seen in, for example, 4S are likely
- What is the relation between B-vitamins and cancer? (Hypomethylation from folate deficiency increasing gene expression vs “feeding” rapidly-dividing cells with folate). Findings NOT significant in NORVIT; ongoing surveillance wise in future trials
- Although lack of proof of benefit does not prove no benefit, we cannot advocate the use of B vitamins in post MI subjects at this time
- The relationship between Hcy and vascular disease cannot, so far, be established as causal