



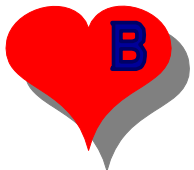
WENBIT

Western Norway B-vitamin Intervention Trial

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The WENBIT Study Group



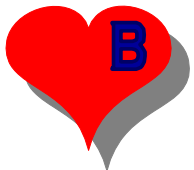
Background and Objectives

Background

- Homocysteine-hypothesis of vascular disease
- Vitamin B₆ status cardiovascular risk modifier

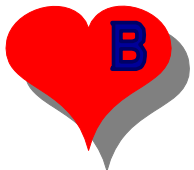
Objectives

To study the effect of homocysteine-lowering therapy with folic acid + vitamin B₁₂, and the separate effect of vitamin B₆ therapy, on mortality and cardiovascular events in patients undergoing coronary angiography.



Study Population

3090 patients with stable angina (84%), ACS (15%) or aortic valve stenosis (1%), undergoing coronary angiography at Bergen or Stavanger University Hospitals, 1999 – 2004

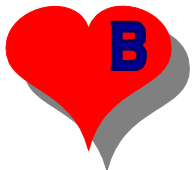


Sample Size Calculation

Sample size $N=3088$ to give 80% power to detect 20% difference if

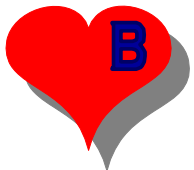
- follow-up 4 years
- 4-year total event rate 22%
- drop-outs $\leq 20\%$

at a 5% significance level



Intervention Groups

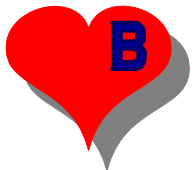
	Folic acid + vitamin B ₁₂	Non- folic acid
Vitamin B ₆	Folic acid (0.8 mg) +B12 (0.4 mg) +B6 (40 mg) N=771	B6 (40 mg) N=771
Non- vitamin B ₆	Folic acid (0.8 mg) +B12 (0.4 mg) N=769	Placebo N=779



Primary End Point

A composite of

- death (all cause)
- non-fatal acute myocardial infarction
- acute hospitalisation for unstable angina
 - with ECG signs of acute ischemia and/or
 - with angiographically verified progression
- non-fatal thromboembolic stroke



Baseline Characteristics – 1

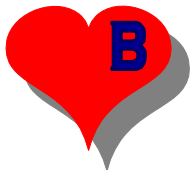
	Folic Acid +B12 +B6	Folic Acid +B12	B6	Placebo
Age – yr ±SD	61.7 ±10.3	61.3 ±10.0	61.4 ±9.7	62.0 ±9.9
Male sex – %	81.2	80.4	80.2	76.5
Reduced LVEF ≤0.5 – %	14.9	13.9	15.6	14.4
Cholesterol – mmol/L ±SD	5.1 ±1.1	5.1 ±1.3	5.1 ±1.2	5.1 ±1.2
Prior chol. ≥6.5 mmol/L – %	58.2	58.6	60.7	59.2
Hypertension – %	45.4	46.3	45.7	47.8
Current smoker – %	28.4	26.4	30.9	27.6

Baseline Characteristics – 2

	Folic Acid +B12 +B6	Folic Acid +B12	B6	Placebo
Prior MI – %	37.9	42.0	43.1	42.9
Prior PCI – %	19.7	20.4	21.0	21.4
Prior CABG – %	14.7	11.3	14.1	13.6
1-vessel disease – %	29.1	29.5	31.3	29.3
2-vessel disease – %	27.0	26.7	25.7	27.5
3-vessel disease – %	33.1	33.2	31.9	32.0
PCI at baseline – %	44.6	45.5	43.5	42.5
CABG at baseline – %	23.0	25.7	24.3	22.2

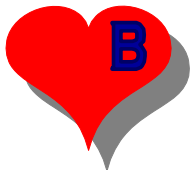
Baseline Characteristics – 3

	Folic Acid +B12 +B6	Folic Acid +B12	B6	Placebo
Acetylsalicylic acid – %	89.0	90.8	90.0	90.9
Clopidogrel – %	23.6	25.5	26.7	24.1
Statins – %	88.1	87.0	89.8	88.6
Beta-blockers – %	77.3	80.0	78.9	76.5
ACE inhibitors – %	18.8	23.4	21.0	22.3
AT II antagonists – %	11.5	9.1	10.2	12.7



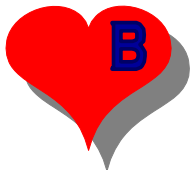
Baseline Vitamin Status

- No mandatory folic acid fortification of foods in Norway
- 19% used B-vitamin supplements containing small doses of folic acid
- Supplement users had somewhat lower total homocysteine levels (10.6 $\mu\text{mol/L}$) than non-users (10.8 $\mu\text{mol/L}$), $p=0.02$



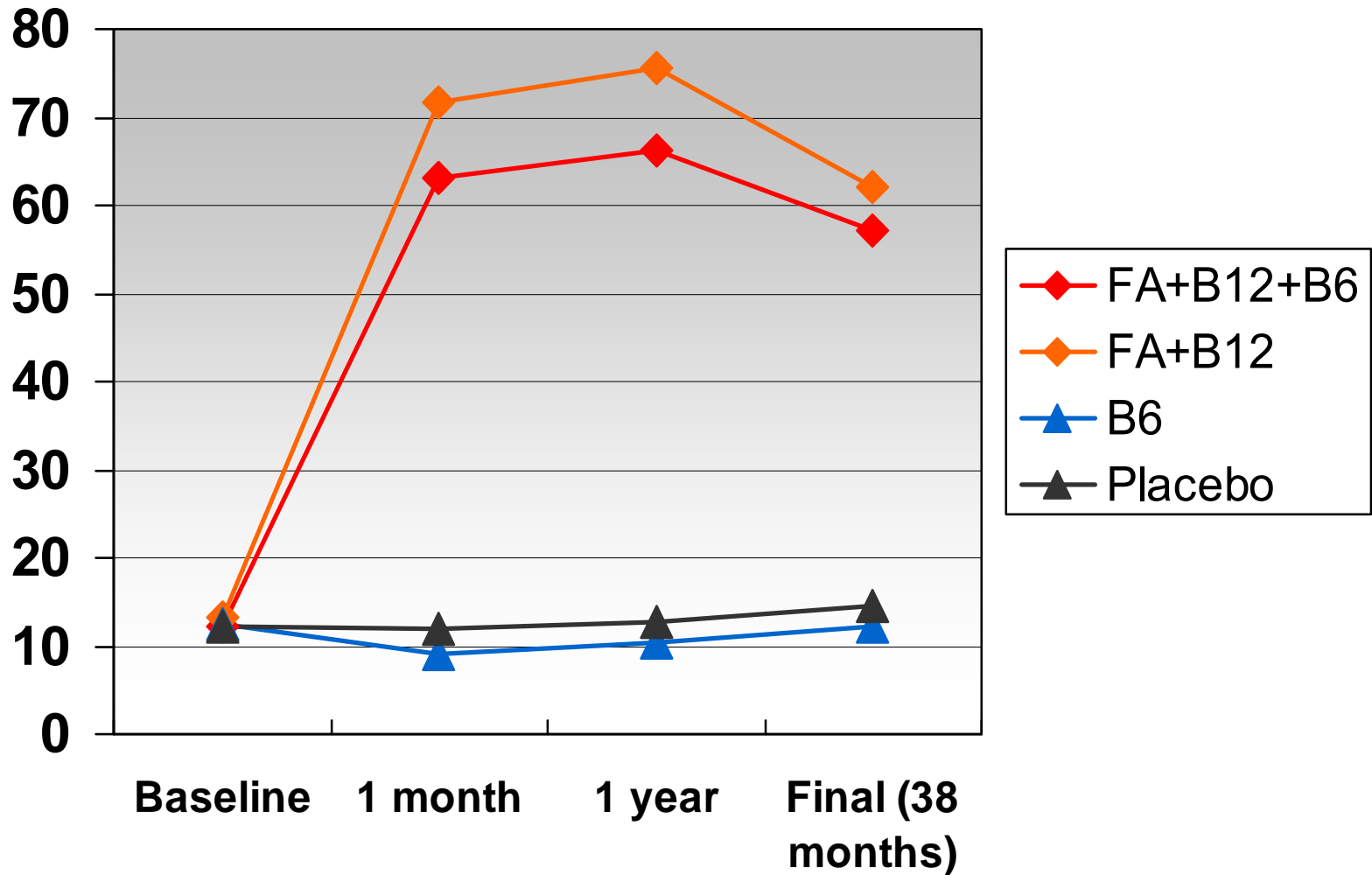
Follow-up

- Study visits at 1 month, 12 months and final after median follow-up time 38 months.
- 18% drop-outs, no significant differences in drop-out rates.
- Intervention terminated ahead of schedule for 22% of participants October 2005
- 422 participants (13.7%) with events classified as the primary end point (intention to treat).



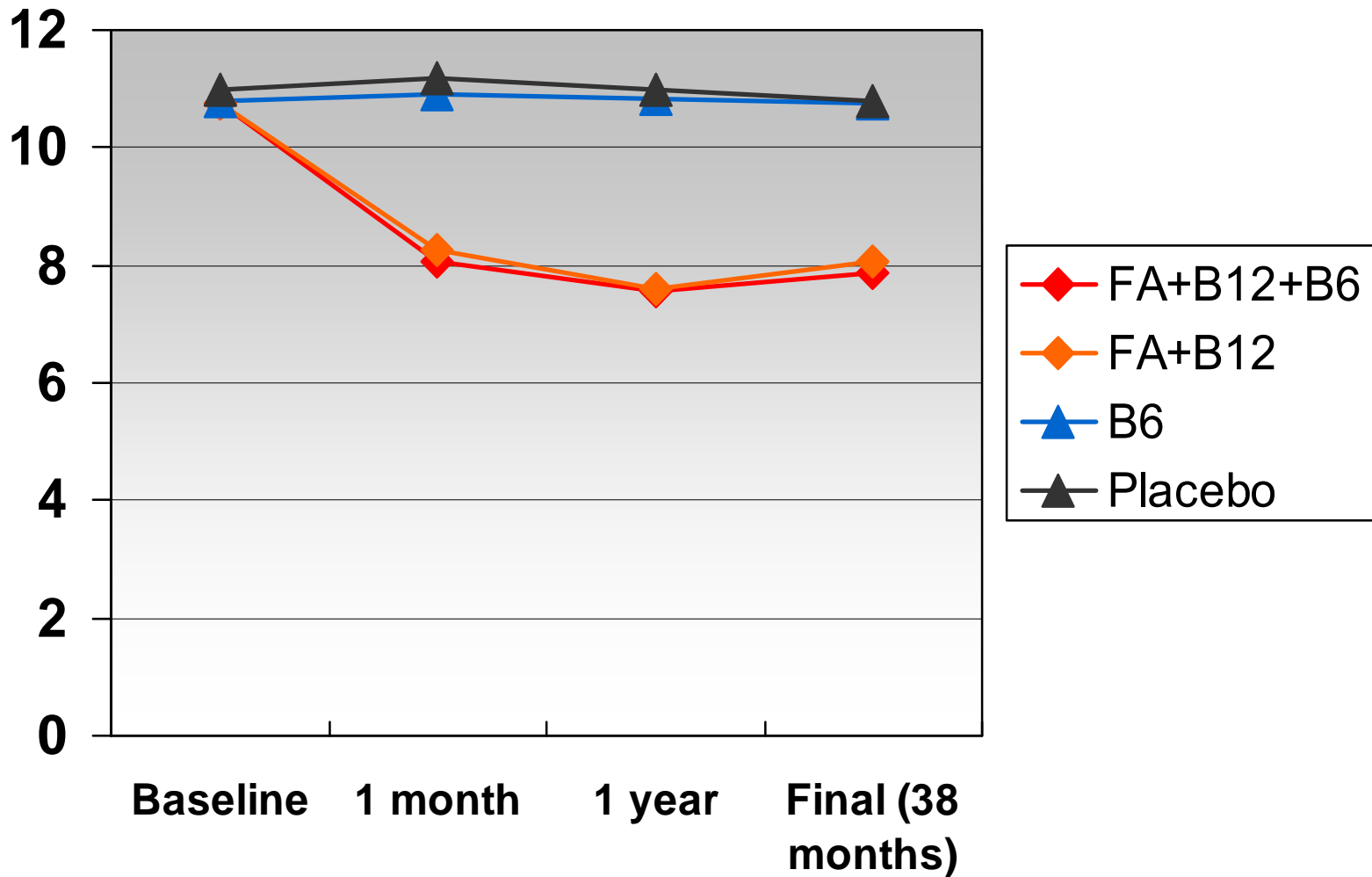
Folate Levels

s-Fol – nmol/L



Homocysteine-lowering

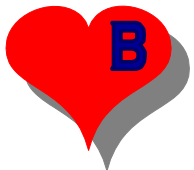
tHcy – $\mu\text{mol/L}$



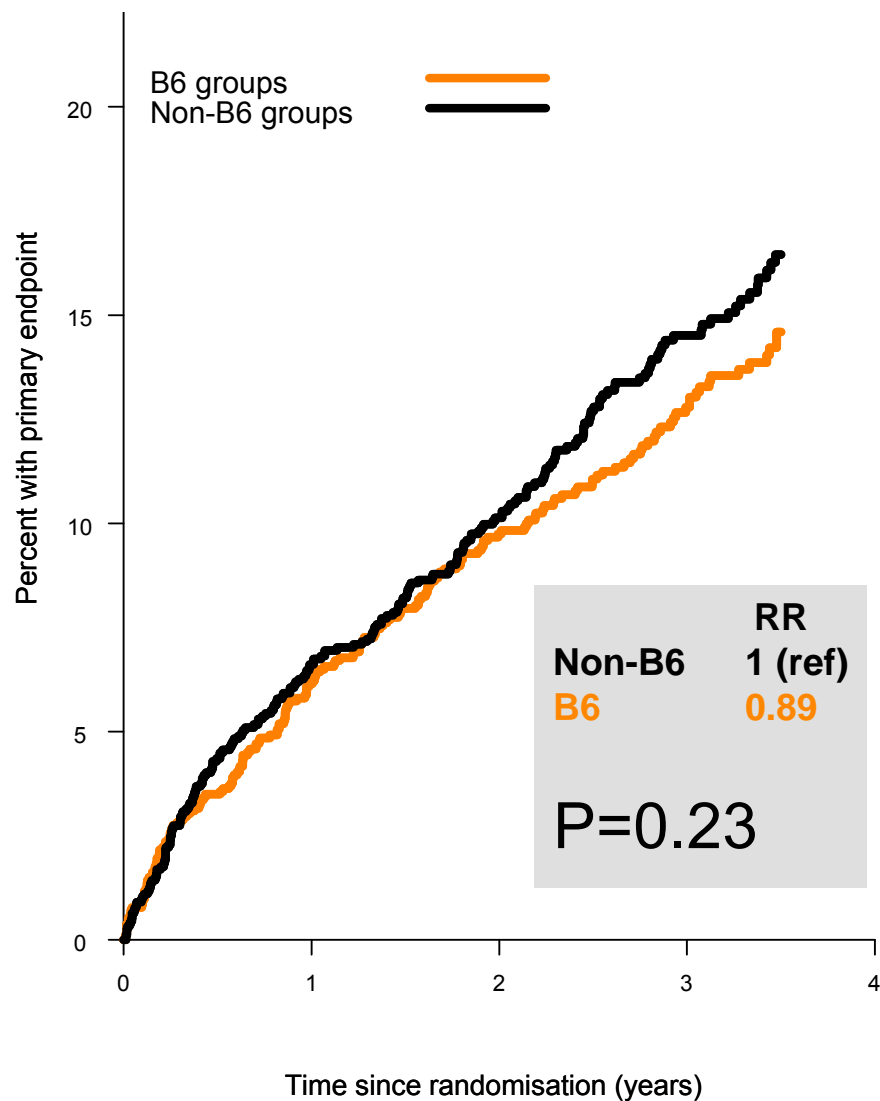
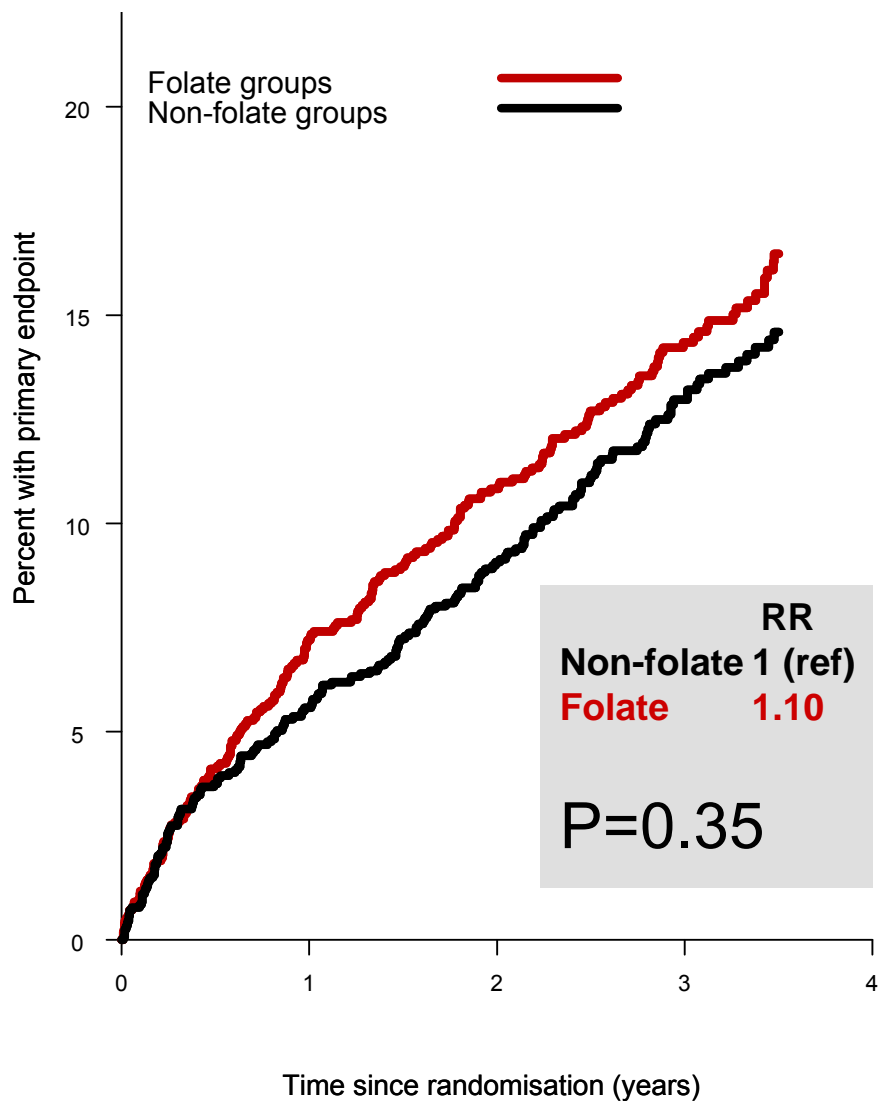
Events in Primary End Point*

	Folic Acid +B12 +B6	Folic Acid +B12	B6	Placebo	Total
All cause death	31	33	28	25	117
Non-fatal AMI	35	50	43	34	162
Unstable angina	18	27	20	22	87
Stroke	9	16	15	16	56
Total	93	126	106	97	422

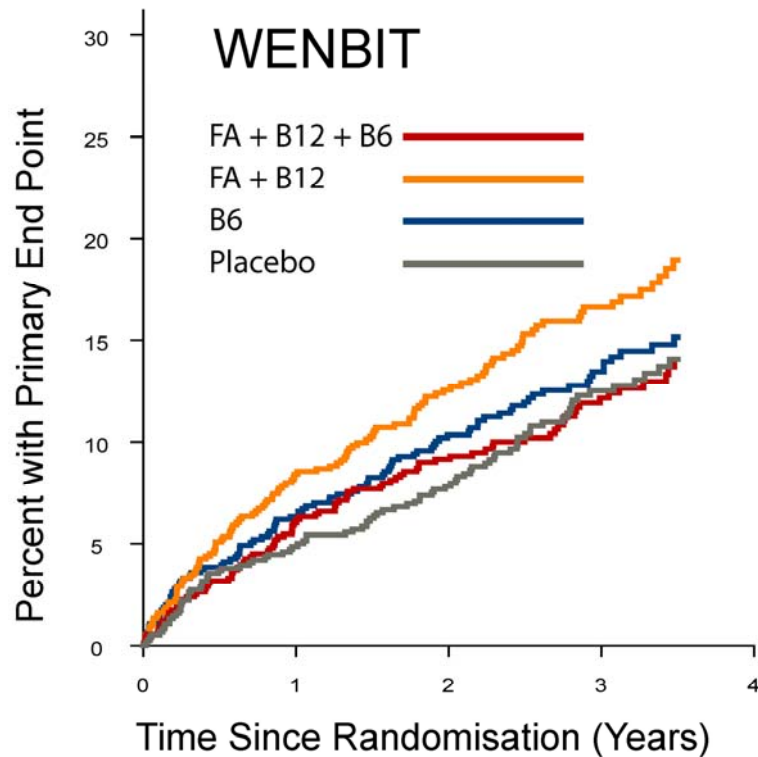
*Numbers



Primary End Point – 422 Events

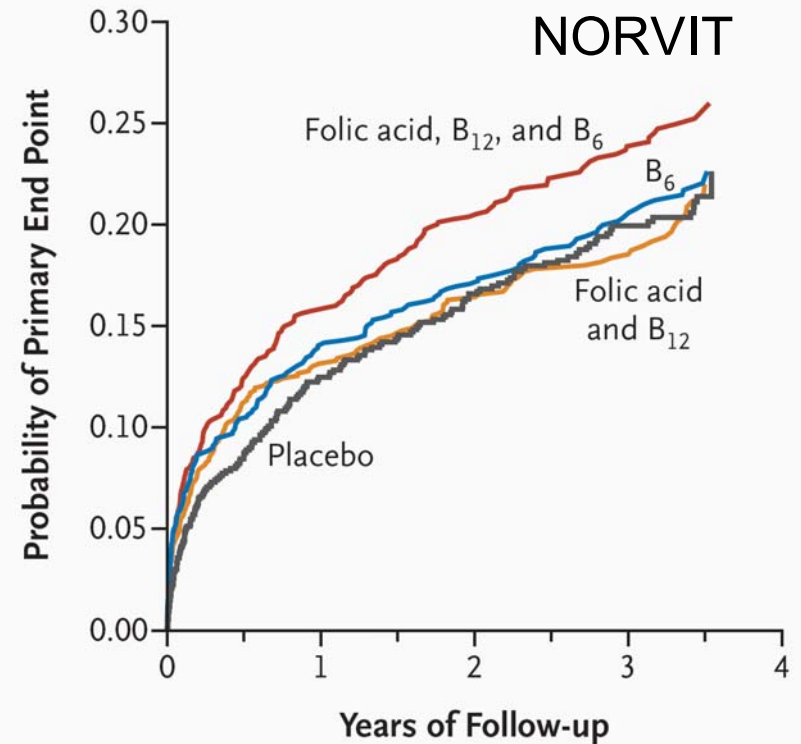


Norwegian Secondary Prevention Trials with Identical B-vitamin Intervention



No. at Risk

	0	1	2	3	4
FA+B12+B6	772	727	649	409	
FA+B12	770	708	616	425	
B6	772	725	624	422	
Placebo	780	743	650	425	

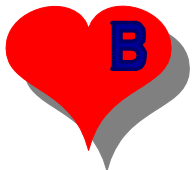


No. at Risk

	0	1	2	3	4
Folic acid, B ₁₂ , and B ₆	937	795	745	517	
Folic acid and B ₁₂	935	812	764	518	
B ₆	934	805	766	511	
Placebo	943	823	771	523	

WENBIT

- Large B-vitamin intervention trial in population with mainly stable angina and 2 or 3 vessel CAD, without folic acid fortification of foods.
- Homocysteine-lowering effect as expected
- No significant difference in primary end point (death and cardiovascular events) between folate and non-folate or B₆ and non-B₆ groups.



WENBIT Organisation

Steering Committee

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Prof. Per Magne Ueland²

Prof. Stein Emil Vollset³

Prof. Helga Refsum⁴

Prof. Dennis Nilsen⁵

Prof. Ottar Nygard^{1,2}

End-points Committee

Prof. Per Lund-Johansen²

MD Leik Woie⁵

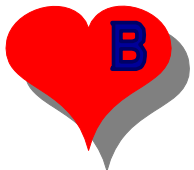
MD Marta Ebbing^{1,2}

Safety Committee

Prof. Rolv T Lie³

Prof. Terje R Pedersen⁶

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