

# Abstract

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## Mortality and cardiovascular events in patients treated with homocysteine-lowering B vitamins after coronary angiography: a randomized controlled trial.

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**CONTEXT:** Observational studies have reported associations between circulating total homocysteine concentration and risk of cardiovascular disease. Oral administration of folic acid and vitamin B(12) can lower plasma total homocysteine levels.

**OBJECTIVE:** To assess the effect of treatment with folic acid and vitamin B(12) and the effect of treatment with vitamin B(6) as secondary prevention in patients with coronary artery disease or aortic valve stenosis.

**DESIGN, SETTING, AND PARTICIPANTS:** Randomized, double-blind controlled trial conducted in the 2 university hospitals in western Norway in 1999-2006. A total of 3096 adult participants undergoing coronary angiography (20.5% female; mean age, 61.7 years) were randomized. At baseline, 59.3% had double- or triple-vessel disease, 83.7% had stable angina pectoris, and 14.9% had acute coronary syndromes.

**INTERVENTIONS:** Using a 2 x 2 factorial design, participants were randomly assigned to 1 of 4 groups receiving daily oral treatment with folic acid, 0.8 mg, plus vitamin B(12), 0.4 mg, plus vitamin B(6), 40 mg (n = 772); folic acid plus vitamin B(12) (n = 772); vitamin B(6) alone (n = 772); or placebo (n = 780).

**MAIN OUTCOME MEASURES:** The primary end point was a composite of all-cause death, nonfatal acute myocardial infarction, acute hospitalization for unstable angina pectoris, and nonfatal thromboembolic stroke.

**RESULTS:** Mean plasma total homocysteine concentration was reduced by 30% after 1 year of treatment in the groups receiving folic acid and vitamin B(12). The trial was terminated early because of concern among participants due to preliminary results from a contemporaneous Norwegian trial suggesting adverse effects from the intervention. During a median 38 months of follow-up, the primary end point was experienced by a total of 422 participants (13.7%): 219 participants (14.2%) receiving folic acid/vitamin B(12) vs 203 (13.1%) not receiving such treatment (hazard ratio, 1.09; 95% confidence interval, 0.90-1.32; P = .36) and 200 participants (13.0%) receiving vitamin B(6) vs 222 (14.3%) not receiving vitamin B(6) (hazard ratio, 0.90; 95% confidence interval, 0.74-1.09; P = .28).

**CONCLUSIONS:** This trial did not find an effect of treatment with folic acid/vitamin B(12) or vitamin B(6) on total mortality or cardiovascular events. Our findings do not support the use of B vitamins as secondary prevention in patients with coronary artery disease.

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