

# Abstract

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## Homocysteine lowering with folic acid and B vitamins in vascular disease.

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**BACKGROUND:** In observational studies, lower homocysteine levels are associated with lower rates of coronary heart disease and stroke. Folic acid and vitamins B6 and B12 lower homocysteine levels. We assessed whether supplementation reduced the risk of major cardiovascular events in patients with vascular disease.

**METHODS:** We randomly assigned 5522 patients 55 years of age or older who had vascular disease or diabetes to daily treatment either with the combination of 2.5 mg of folic acid, 50 mg of vitamin B6, and 1 mg of vitamin B12 or with placebo for an average of five years. The primary outcome was a composite of death from cardiovascular causes, myocardial infarction, and stroke.

**RESULTS:** Mean plasma homocysteine levels decreased by 2.4 micromol per liter (0.3 mg per liter) in the active-treatment group and increased by 0.8 micromol per liter (0.1 mg per liter) in the placebo group. Primary outcome events occurred in 519 patients (18.8 percent) assigned to active therapy and 547 (19.8 percent) assigned to placebo (relative risk, 0.95; 95 percent confidence interval, 0.84 to 1.07;  $P=0.41$ ). As compared with placebo, active treatment did not significantly decrease the risk of death from cardiovascular causes (relative risk, 0.96; 95 percent confidence interval, 0.81 to 1.13), myocardial infarction (relative risk, 0.98; 95 percent confidence interval, 0.85 to 1.14), or any of the secondary outcomes. Fewer patients assigned to active treatment than to placebo had a stroke (relative risk, 0.75; 95 percent confidence interval, 0.59 to 0.97). More patients in the active-treatment group were hospitalized for unstable angina (relative risk, 1.24; 95 percent confidence interval, 1.04 to 1.49).

**CONCLUSIONS:** Supplements combining folic acid and vitamins B6 and B12 did not reduce the risk of major cardiovascular events in patients with vascular disease. (ClinicalTrials.gov number, NCT00106886)

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