

Abstract

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Effects of lowering homocysteine levels with B vitamins on cardiovascular disease, cancer, and cause-specific mortality: Meta-analysis of 8 randomized trials involving 37 485 individuals.

Clarke R, Halsey J, Lewington S, Lonn E, Armitage J, Manson JE, Bønaa KH, Spence JD, Nygård O, Jamison R, Gaziano JM, Guarino P, Bennett D, Mir F, Peto R, Collins R; B-Vitamin Treatment Trialists' Collaboration: Mir F, Brown M, Lonn E, Yusuf S, Bønaa KH, Njolstad I, Armitage J, Bowman L, Clarke R, Parish S, Peto R, Collins R, Jamison R, Gaziano JM, Guarino P, Toole J, Malinow MR, Pettigrew LC, Spence JD, Howard VJ, Sides EG, Wang CH, Stampfer M, Manson JE, Glynn R, Grodstein F, Albert CM, Cook NR, Nygård O, Ebbing M, Nordrehaug JE, Nilsen DW, Refsum H, Vollset SE, Clarke R, Halsey J, Lewington S, Bennett D, Collins R.

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OBJECTIVE: Elevated plasma homocysteine levels have been associated with higher risks of cardiovascular disease, but the effects on disease rates of supplementation with folic acid to lower plasma homocysteine levels are uncertain.

METHODS: Individual participant data were obtained for a meta-analysis of 8 large, randomized, placebo-controlled trials of folic acid supplementation involving 37 485 individuals at increased risk of cardiovascular disease. The analyses involved intention-to-treat comparisons of first events during the scheduled treatment period.

RESULTS: There were 9326 major vascular events (3990 major coronary events, 1528 strokes, and 5068 revascularizations), 3010 cancers, and 5125 deaths. Folic acid allocation yielded an average 25% reduction in homocysteine levels. During a median follow-up of 5 years, folic acid allocation had no significant effects on vascular outcomes, with rate ratios (95% confidence intervals) of 1.01 (0.97-1.05) for major vascular events, 1.03 (0.97-1.10) for major coronary events, and 0.96 (0.87-1.06) for stroke. Likewise, there were no significant effects on vascular outcomes in any of the subgroups studied or on overall vascular mortality. There was no significant effect on the rate ratios (95% confidence intervals) for overall cancer incidence (1.05 [0.98-1.13]), cancer mortality (1.00 [0.85-1.18]) or all-cause mortality (1.02 [0.97-1.08]) during the whole scheduled treatment period or during the later years of it.

CONCLUSIONS: Dietary supplementation with folic acid to lower homocysteine levels had no significant effects within 5 years on cardiovascular events or on overall cancer or mortality in the populations studied.

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