

Homocysteine, B Vitamins, and Cardiovascular Disease

TO THE EDITOR: The HOPE-2 investigators show a significant, 24 percent reduction in the relative risk of stroke among patients treated with folic acid and vitamins B₆ and B₁₂. They downplay this result by relegating a striking figure on the effect of this treatment on stroke (Fig. 1) to their online Supplementary Appendix. The authors suggest that the result may be spurious, but it agrees closely with the predictions of two large meta-analyses, which suggested that the same change in homocysteine levels achieved in the HOPE-2 trial would result in a reduction in stroke of 19 to 24 percent.^{1,2} Their view — that a treatment benefit restricted to stroke is biologically implausible — is surprising, given the etiologic differences in coronary disease and stroke. They claim that the findings of the Vitamin Intervention for Stroke Prevention (VISP)³ and NORVIT studies support their conclusion. However, they did not refer to the reanalysis of the VISP trial, which revealed a significant effect on stroke and coronary events.⁴ They also did not mention that the NORVIT study was smaller, with a total of 98 strokes, as compared with 258 strokes in their own trial.

The message of the HOPE-2 trial should be one of cautious optimism that B vitamins may protect against stroke. Consistent with this view is a reduction in the rate of death from stroke in the United States and Canada after the introduction of folic acid fortification of food.⁵

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