

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: The Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators. Homocysteine lowering with folic acid and B vitamins in vascular disease. *N Engl J Med* 2006;354:1567-77.

Additional Table and Figure for Electronic Supplementary Appendix

Table. Eligibility Criteria for the HOPE-2 Trial

Inclusion criteria	
	<ul style="list-style-type: none">Women and men 55 years and above with any of the following:
Coronary artery disease	<p>Previous myocardial infarction (> 1 month before randomization)</p> <p>Stable or unstable angina with documented multivessel CAD (by angiography or stress test)</p> <p>Previous multivessel percutaneous coronary intervention (> 1 month before randomization)</p> <p>Multivessel coronary artery bypass graft surgery (> 4 years before randomization or with recurrence of angina)</p> <p>Multivessel coronary disease on coronary angiography (>50% stenosis in ≥ 2 arteries)</p>
Peripheral arterial disease	<p>Previous limb bypass surgery or percutaneous transluminal intervention</p> <p>Intermittent claudication with ankle/arm BP ratio ≤ 0.80 on at least one side</p> <p>Significant peripheral artery stenosis (>50%) documented by angiography</p> <p>Previous ischemic limb or foot amputation</p>
Cerebrovascular disease	<p>Previous stroke (> 1 month prior to randomization)</p>

Diabetes mellitus with at least one additional risk factor:

- Previous endarterectomy
- Hypertension (BP >160 mmHg systolic or >90 mmHg diastolic or on treatment)
- Total cholesterol >5.2 mmol/L
- HDL cholesterol <0.9 mmol/L
- Current cigarette smoking
- Known microalbuminuria
- Evidence of atherothrombotic vascular disease

- Provision of informed consent

Exclusion criteria

- Current use of vitamin supplements containing folic acid >200µg/day
- Known previous adverse reactions to folic acid and/or vitamins B₆ and/or B₁₂
- Planned cardiac, peripheral or cerebrovascular revascularization, defined as decision to perform surgical or percutaneous transluminal revascularization within the next 6 months
- Clinically significant non-atherothrombotic cardiovascular disease, defined as advanced valvular disease, advanced pericardial disease, complex congenital heart disease, cor pulmonale, advanced cardiomyopathy, heart transplant

recipient)

- Other important non-cardiovascular disease expected to limit compliance and/or impact on patient's ability to comply with the study protocol and complete the study, such as history of alcohol abuse, psychiatric disorders, senility, severe physical disability, including terminal stage of cancer and other major systemic illnesses

Supplemental Figure for the Website

