Vitamin E not helpful, perhaps harmful

Clinical question In patients with or without heart disease, does vitamin E supplementation decrease mortality?

Bottom line Vitamin E supplementation does not decrease all-cause mortality in patients with or without pre-existing heart disease. At higher doses it can actually be harmful, although the deleterious effect is small (number needed to treat to harm = 250). (Level of evidence = 1b)

Miller ER III, Pastor-Barriuso R, Dalal D, et al. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med*. 2005;142:37-46.

Study Design Meta-analysis (randomized controlled trials)

Setting Outpatient (any)

Synopsis The antioxidant property of vitamin E has led many to use it to prevent cardiovascular or cancer-related mortality. However, several studies and several previous meta-analyses have shown either no benefit or a slight increase in mortality with its use. The authors of this study performed a literature search in the usual way, searching MEDLINE, the Cochrane Clinical Trials Database, and reference lists and files. They included 19 randomized studies of almost 136,000 patients comparing vitamin E with a control or placebo group for at least 1 year and with at least 10 deaths in the trial. Study subjects varied and included elderly patients, healthy adults, and patients with cardiovascular disease. Study results were analyzed by intention to treat. The method of data extraction was not explained and studies were not graded or selected on the basis of quality. In the studies, the baseline death rate was approximately 10%. Overall, there was no difference in all-cause mortality between the control group and placebo group. However, when comparing low-dose versus high-dose vitamin E (less than 400 IU/day versus 400 IU/day or more), differences were found. In the studies of lower doses, there was no benefit or detriment to vitamin E supplementation (relative risk = 0.98; 95% CI, 0.96-1.01). When high-dose supplementation was studied separately, the risk was slightly but significantly higher in the supplemented group, with a number needed to treat to harm of 250 (143 998). The effect of vitamin E supplementation was not different when the results were evaluated by patient's sex or average age or by the length of follow-up.

Rivastigmine of some benefit in Parkinson's disease with dementia

Clinical question Is rivastigmine an effective drug for the treatment of dementia in patients with Parkinson's disease?

Bottom line Rivastigmine (Exelon) provides a small benefit in patients with Alzheimer's disease and Parkinson's disease at a cost of increased nausea, vomiting, and tremor. The decision to use rivastigmine should be personalized and the drug should be discontinued if patients do not experience a clear benefit. (Level of evidence = 1b)

Emre M, Aarsland D, Albanese A, et al. Rivastigmine for dementia associated with Parkinson's disease. *N Engl J Med*. 2004;351:2509-2518.

Study Design Randomized controlled trial (double-blinded)

Setting Outpatient (specialty)

Synopsis Dementia is relatively common in patients with Parkinson's disease, with a cumulative prevalence of up to 80%. Rivastigmine is an acetylcholinesterase and butyryl cholinesterase inhibitor that has been shown to be effective in dementia with Lewy bodies, a condition that overlaps with dementia in Parkinson's disease. In this study, 541 patients were randomized in a 2:1 ratio to either rivastigmine in an escalating dose of 3 mg to 12 mg as tolerated or matching placebo. Patients were followed for up to 24 weeks, allocation was concealed, outcomes were blindly assessed, and analysis was by intention to treat with the last observation carried forward. More patients dropped out of the study in the rivastigmine group, even when accounting for the 2:1 allocation (99 versus 32). Adverse events (especially nausea, vomiting, and worsening tremor) and withdrawal of consent were the major factors. Compared with those taking placebo, patients taking rivastigmine had small but statistically significant benefits on a variety of tests of cognition. However, the change in the cognitive subscale of the Alzheimer's Disease Assessment Scale after 24 weeks was -2.1 for those taking rivastigmine compared with an increase of 0.7 in those taking placebo (higher scores are worse). This represents a change of 2.8 points on a 70-point scale, with a baseline score of approximately 24, and is of questionable clinical significance. Other scores demonstrated similarly small benefits.

Fecal DNA testing more sensitive than Hemoccult II

Clinical question Is a fecal DNA test better than the standard Hemoccult II fecal occult-blood test at detecting important colorectal lesions?

Bottom line Fecal DNA testing is more sensitive than the traditional Hemoccult II, although it is also much more expensive and is less sensitive than colonoscopy. (Level of evidence = 1b)

Imperiale TF, Ransohoff DF, Itzkowitz SH, et al; Colorectal Cancer Study Group. Fecal DNA versus fecal occult blood for colorectal-cancer screening in an average-risk population. *N Engl J Med*. 2004;351:2704-2714.

Study Design Cross-sectional

Setting Outpatient (any)

Synopsis Fecal DNA testing looks for evidence of mutations in a handful of genes associated with the majority of colorectal cancers. The authors identified an asymptomatic group of subjects older than 50 years (at least 75% were older than 65 years). The mean age was 69 years, 44% were men, and 87% were white. Each subject was asked to provide a stool sample for fecal DNA testing, to complete 3 Hemoccult II cards with a total of 6 panels following dietary and medication modification and mail them to the research center for unrehydrated analysis, and to schedule a colonoscopy. No dietary modification is needed for the fecal DNA testing. Of the original group of 5486 recruits, 4404 were included in the study group; others were excluded because they could not provide a stool sample, did not complete the Hemoccult II cards, or did not have the colonoscopy. Blinding was incomplete: The fecal DNA laboratory was blinded to colonoscopy results and vice versa, but the colonoscopists could have learned the Hemoccult II test results if they desired. Of the original group of 4404, 2318 had no polyps, 1627 had minor polyps, 426 had advanced adenomas, and 33 had carcinoma. The researchers then saved some money by taking a random sample of those with minor polyps and no polyps and performed the fecal DNA testing only on that subset, plus all patients with confirmed advanced adenomas or adenocarcinoma. The fecal DNA test had similar specificity to the Hemoccult II (94.4% versus 95.2%) but was significantly more sensitive for the detection of adenocarcinoma (51.6% versus 12.9%), node negative adenocarcinoma (56% versus 13%), and TNM stage I, II, or III adenocarcinoma (40.8% versus 14.1%). The positive and negative likelihood ratios were 10.3 and 0.6 for fecal DNA compared with 2.7 and 1.0 for Hemocccult II in the detection of adenocarcinoma. Fecal DNA testing was also significantly more sensitive for the detection of adenomas with high-grade dysplasia (32.5% versus 15.0%) but no better in its ability to detect other advanced adenomas. For the combined outcome of advanced adenoma or cancer, the fecal DNA test was significantly more sensitive (18.2% versus 10.8%). The test is estimated to cost between $400 and $800.