POEMs®
PATIENT ORIENTED EVIDENCE THAT MATTERS
Practice Recommendations from Key Studies

Vitamin E not helpful, perhaps harmful

Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med 2005; 142:37–46.

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 harm [NNH]=250). (level of evidence [LOE]=**1b**)

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 patient 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 with high-dose vitamin E (less than 400 IU/d vs 400 IU/d 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% confidence interval [CI], 0.96–1.01). When high-dose supplementation was studied separately, the risk was slightly but significantly higher in the supplemented group

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What is a POEM?

Each month, the POEMs (Patient-Oriented Evidence that Matters) editorial team reviews 105 research journals in many specialties, and selects and evaluates studies that investigate important primary care problems, measure meaningful outcomes, and have the potential to change the way medicine is practiced. Each POEM offers a Bottom Line observation and summarizes the study's objective, patient population, study design and validity, and results. InfoPOEMs, Info-Retriever and POEMS for Primary Care are registered trademarks of InfoPOEM, Inc. POEMS and Patient-Oriented Evidence that Matters are trademarks of InfoPOEM, Inc.

(NNH=250; 95% CI, 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.

Acupuncture effective for osteoarthritis of the knee

Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. Ann Intern Med 2004; 141:901–910.

CLINICAL QUESTION

Is acupuncture effective in decreasing pain and improving function in patients with osteoarthritis of the knee?

BOTTOM LINE

Acupuncture, as compared with sham acupuncture treatment or no treatment, decreases pain scores by an average of 40% and improves function similarly in patients who stick with it. The acupuncture used in this study was based on the Traditional Chinese Medicine meridian theory and was used for the entire 6 months of the study. (LOE=**1b**)

STUDY DESIGN

Randomized controlled trial (double-blinded)

ALLOCATION

Concealed

SETTING

Outpatient (any)

SYNOPSIS

This is the largest and most rigorous study to date of the effect of acupuncture in the treatment of osteoarthritis. The authors enrolled 570 patients who had radiologic and clinical evidence of osteoarthritis of the knee and who had not had any intra-articular injections.

The patients were assigned to 1 of 3 treatment groups: (1) "true acupuncture" based on Traditional Chinese Medicine meridian theory to treat knee joint pain; (2) a sham treatment that mimicked true acupuncture, except that the needles weren't actually inserted (the acupuncture guiding tubes were tapped at sham points, followed by affixing needles, without insertion, at these sites with adhesive tape); and (3) a control group that received six 2-hour group education sessions lead by a patient education specialist, with follow-up mailed educational materials. Treatment was rendered twice a week for 8 weeks, tapering over the next month to 1 treatment per month, which was continued through the end of the study. This design addresses 2 issues that have plagued previous acupuncture research by providing a sham-treatment as well as a no-treatment group.

At week 14, pain scores using the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) decreased from an initial average score of 8.9 (of a possible 20) by 3.6 units (40% improvement) in the true acupuncture group compared with a 2.7-unit increase in the sham group and a 1.5-unit decrease in the education group. This change with true acupuncture was statistically significant compared with the other 2 groups.

Pain scores continued to improve in all 3 groups over the course of the study, though true acupuncture scores continued to improve statistically more than the other 2 groups. Functional deficit diminished from an average 32 units (of a possible 68 at baseline) to 19 units at the end of the study, an almost 40% improvement that was statistically better than the other 2 groups. Patient global assessment scores also improved in the acupuncture group to a statistically greater extent than in either other group. Distance during the 6-minute walk and 36-Item Short-Form Health Survey scores improved more with true and sham acupuncture treatment than with education, but the results were similar between those 2 groups.

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PATIENT ORIENTED EVIDENCE THAT MATTERS

Use CCBs as last resort in treatment of hypertension

Wassertheil-Smoller S, Psaty B, Greenland P, et al. Association between cardiovascular outcomes and antihypertensive drug treatment in older women. JAMA 2004; 292:2849–2859.

CLINICAL QUESTION

In the treatment of adults with hypertension, which other drug class added to diuretics most effectively reduces adverse cardiovascular events?

BOTTOM LINE

In women with hypertension and no history of cardiovascular disease (CVD), a regimen of a diuretic plus either a beta-blocker or angiotensin-converting enzyme (ACE) inhibitor reduces the risk of CVD mortality compared with a diuretic plus calcium channel blocker. The evidence continues to mount that calcium channel blockers should be the agent of last resort in the treatment of most patients with hypertension. (LOE=**2b–**)

STUDY DESIGN

Cohort (prospective)

SETTING

Population-based

SYNOPSIS

Evidence shows that diuretics are equal to or superior to other agents as first-line therapy for most patients with hypertension. More than 1 drug class, however, is frequently required to control hypertension. It is unclear which other drug classes, added to diuretics, optimally reduce adverse cardiovascular events.

The investigators evaluated data obtained from women with hypertension enrolled in the Women's Health Initiative Observational Study, a prospective cohort study of 93,676 women aged 50 to 79 years at baseline. Of these, 94% were

THE JOURNAL OF FAMILY PRACTICE

Evidence-based medicine ratings

THE JOURNAL OF FAMILY PRACTICE uses a simplified rating system system called the Strength of Recommendation Taxonomy (SORT). More detailed information can be found in the February 2003 issue, "Simplifying the language of patient care," pages 111–120.

Strength of Recommendation (SOR) ratings are given for key recommendations for readers. SORs should be based on the highest-quality evidence available.

- **A** Recommendation based on consistent and good-quality patient–oriented evidence.
- **B** Recommendation based on inconsistent or limited-quality patient-oriented evidence.
- **C** Recommendation based on consensus, usual practice, opinion, disease-oriented evidence, or case series for studies of diagnosis, treatment, prevention, or screening

Levels of evidence determine whether a study measuring patient-oriented outcomes is of good or limited quality, and whether the results are consistent or inconsistent between studies.

STUDY QUALITY

1—Good-quality, patient-oriented evidence (eg, validated clinical decision rules, systematic reviews and meta-analyses of randomized controlled trials [RCTs] with consistent results, high-quality RCTs, or diagnostic cohort studies)

2—Lower-quality patient-oriented evidence (eg, unvalidated clinical decision rules, lower-quality clinical trials, retrospective cohort studies, case control studies, case series)

3—Other evidence (eg, consensus guidelines, usual practice, opinion, case series for studies of diagnosis, treatment, prevention, or screening)

Consistency across studies

Consistent—Most studies found similar or at least coherent conclusions (coherence means that differences are explainable); *or* If high-quality and up-to-date systematic reviews or meta-analyses exist, they support the recommendation

Inconsistent—Considerable variation among study findings and lack of coherence; *or* If high-quality and up-to-date systematic reviews or meta-analyses exist, they do not find consistent evidence in favor of the recommendation

followed up for a mean of 5.9 years. Antihypertensive medication was determined from original bottles brought to baseline visits and matched to a pharmacy database. Endpoints were ascertained from mailed questionnaires, direct report, telephone follow-up, medical records, and death certificates. The investigators do not specifically state whether outcomes were assessed by individuals blinded to treatment groups.

Among women with hypertension but no history of CVD, monotherapy with calcium channel blockers versus diuretics was associated with an increased risk of CVD death (number needed harm over 6 years [NNH/6]=143; 95% CI, 59–3898). In similar patients, a 2-drug regimen of a diuretic plus calcium channel blocker was associated with a statistically significant increase in CVD death compared with both a diuretic plus beta-blocker and a diuretic plus ACE inhibitor (NNH/6=93; 95% CI, 34–3898). Both analyses were adjusted for age, race/ethnicity, smoking, high cholesterol requiring medication, body mass index, physical activity, hormone use, and diabetes.

Ten years after bariatric surgery: weight loss sustained, diabetes and hypertension reversed

Sjostrom L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004; 351:2683–2693.

CLINICAL QUESTION

How effective is bariatric surgery in the long term?

BOTTOM LINE

Bariatric surgery successfully helps patients lose weight and reverse diabetes, hypertension, and some hyperlipidemias. We still do not know whether it affects all-cause mortality. (LOE=**2c**)

STUDY DESIGN
Non-randomized controlled trial

ALLOCATION
Unconcealed

SETTING
Population-based

SYNOPSIS

A recent meta-analysis found that bariatric surgery successfully treats many of the comorbid conditions associated with obesity. However, most of the studies were of less than 2 years' duration (*JAMA* 2004; 292:1724–1737).

In the current study, Swedish researchers invited patients to undergo bariatric surgery. Of 8966 who met age and weight-for-height criteria, 4047 eventually underwent surgery at 1 of 25 centers. The decision to have surgery was made by the patient after consultation with a surgeon; patients not choosing to have surgery became part of a pool used as control patients. The type of surgery was determined by the physicians at the center. Each patient was matched at the time of surgery with a patient from the control pool based on age, obesity, comorbidities, and other clinical factors. Patients were then followed-up for up to 10 years. Thus, this was not a randomized trial.

The operative mortality rate was 0.25% and the rate of serious surgical complications was 13%. Weight loss peaked after 1 year in the surgery group (38% for gastric bypass, 27% for vertical banded gastroplasty, and 21% for banding). Weight loss at 2 years was an average of 23% for the surgery groups compared with a 0.1% increase in the control group. After 10 years, weight loss was less dramatic (25%, 16%, and 13% for the 3 different procedures), but still better than the 1.6% gain in the control group. At both 2 and 10 years, surgical patients were significantly more likely than controls to have recovered from diabetes (36% vs 13%), hypertension (19% vs 11%), and hypertriglyceridemia (46% vs 24%). There was no difference at either 2 or 10 years in the rate of recovery

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At 2 and 10 years, surgical patients were more likely to have recovered from diabetes and hypertension

from elevated total cholesterol.

The most important outcome, however, is all-cause mortality. The authors do not give these results, as the study is continuing under the watchful eye of a data-monitoring committee, which suggests that there are no important difference between the groups so far.

Guidelines for the treatment of chronic stable angina

Snow V, Barry P, Fihn SD, et al. Primary care management of chronic stable angina and asymptomatic suspected or known coronary artery disease: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2004; 141:562–567.

CLINICAL QUESTION

In patients with chronic stable angina or those who are asymptomatic but who have evidence of coronary artery disease, what is the appropriate medical management?

BOTTOM LINE

In patients who have either chronic stable angina without a history of myocardial infarction or a revascularization procedure in the past 6 months, as well as in asymptomatic patients with demonstrated coronary artery disease, the following should be routine: aspirin; a beta-blocker; an angiotensin-converting enzyme inhibitor; and a statin, if the cholesterol is above normal. (LOE=**1a**)

STUDY DESIGN

Practice guideline

SETTING

Various (guideline)

SYNOPSIS

The American College of Physicians endorses the American College of Cardiology/American Heart Association guidelines from 2002. The guidelines apply to patients with chronic stable angina who have not had a myocardial infarction (MI) or have undergone revascularization in the past 6 months, as well as patients who are asymptomatic but have demonstrated evidence of coronary artery disease. The strength of the recommendations (SOR) are characterized as follows: **A** = several randomized clinical trials with large numbers of patients; **B** = limited number of randomized trials with small numbers of patients, nonrandomized studies, or observational registries; and **C** = expert consensus.

In patients with chronic stable angina or in asymptomatic patients with evidence of coronary artery disease, the following should be routinely used to decrease the risk of MI or death:

- Aspirin 75 to 325 mg daily (SOR: **A**). Clopidogrel (Plavix) should only be used if aspirin is contraindicated (SOR: A). Dipyridamole should not be used because of risk of harm (SOR: **B**).
- A beta-blocker to reduce mortality and MI and to control symptoms (SOR: **A**).
- An angiotensin-converting enzyme inhibitor. An angiotensin receptor blocker should not be substituted (SOR: **A**).
- A statin, if cholesterol is above normal (SOR: **B**).

Symptom control should be managed with:

- Sublingual nitroglycerin (SOR: **A**)
- A long-acting calcium channel blocker or long-acting nitrate when beta-blockers are ineffective or unsuccessful at controlling symptoms (SOR: **B**).

For follow-up (SOR: **C**) the group recommends visits every 4 to 6 months during the first year. Routine cardiac testing is not useful in the absences of a change in history or physical examination.