# POEMs

## Patient-Oriented Evidence that Matters

*If cost alone determined the best antiplatelet therapy for patients with vascular disease, aspirin would win hands down. However, cost is not the only factor as shown by our first POEM, which provides evidence about the use of clopidogrel and dipyridamole in helping to prevent recurrent vascular events without creating unnecessary risk. The second POEM for February should help us to reassure those women under the age of 60 years who have menopausal symptoms but are scared of media reports condemning HRT. We have yet another POEM casting doubt about the benefit of antioxidants and our final POEM reports favourable results for a vaccine for HPV. Editor.*

### Clinical question

Which antiplatelet agents, used alone or in combination, are effective in preventing recurrent vascular events?

### Bottom line

Aspirin is the recommended oral first-line antiplatelet therapy for patients with ST-segment elevation myocardial infarction. Aspirin or clopidogrel is recommended for those with initial transient ischemic attack (TIA)/ischemic stroke, chronic stable angina, or peripheral arterial disease, and aspirin plus clopidogrel should be used for those with non-ST-segment elevation acute coronary syndrome. For second-line therapy, the combination of aspirin and clopidogrel is recommended for recurrent acute coronary syndrome. The combination of aspirin and extended-release dipyridamole is recommended for patients with recurrent TIA/ischemic stroke in the absence of known coronary artery disease. Further studies are needed before making firm recommendations on the management of patients with recurrent TIA/ischemic stroke and known coronary artery disease. (LOE = 1a-)

### Reference

Tran H, Anand SS. Oral antiplatelet therapy in cerebrovascular disease, coronary artery disease, and peripheral arterial disease. JAMA 2004; 292:1867-74.

### Study Design

Systematic review

### Setting

Various (meta-analysis)

### Synopsis

Aspirin prevents recurrent vascular events in a wide range of high-risk patients, but it is unknown if other antiplatelet agents, such as clopidogrel or dipyridamole, alone or in combination with aspirin, are more effective. The investigators rigorously searched multiple databases including MEDLINE, the Cochrane Clinical Trials Registry, and reference lists of trials, review articles, and scientific statements and guidelines of official societies. The authors included randomised trials comparing an antiplatelet regimen to either placebo or another antiplatelet regimen assessing outcomes for at least 10 days. They identified 111 trials enrolling nearly 100 000 patients. The investigators do not state if the search for, and evaluation of, the included studies was done independently by more than one person. No formal assessment of the potential for publication bias was done, nor was any specific analysis done to determine homogeneity of the results. Recommended oral first-line antiplatelet therapy is aspirin for patients with ST-segment elevation myocardial infarction; aspirin or clopidogrel for those with initial transient ischemic attack (TIA)/ischemic stroke, chronic stable angina, or peripheral arterial disease (since aspirin is less expensive, clopidogrel should be reserved only for aspirin-intolerant patients); and aspirin plus clopidogrel for those with non-ST-segment elevation acute coronary syndrome. For second-line therapy, the combination of aspirin and clopidogrel is recommended for recurrent acute coronary syndrome. The combination of aspirin and



** Patient-Oriented Evidence that Matters. See editorial (NZFP 2003; 30:150)*

clopidogrel does not, however, lower the incidence of recurrent vascular events in patients with recurrent TIAs/ischemic stroke, but does increase the risk of major and life-threatening bleeding. The combination of aspirin and extended-release dipyridamole is therefore recommended for patients with recurrent TIA/ischemic stroke in the absence of known coronary artery disease. Because of the theoretical risk of dipyridamole exacerbating myocardial ischemia, further studies are needed before making firm recommendations on the management of patients with both recurrent TIA/ischemic stroke and known coronary artery disease. Ticlopidine is beneficial for various vascular conditions, but frequent side effects – some serious – limit its usefulness.

### Clinical question

Is there a beneficial effect of hormone replacement therapy in younger postmenopausal women?

#### Bottom line

Estrogen replacement in women younger than 60 years, while not affecting individual rates of cardiovascular-related or cancer-related death, results in a net decrease in overall mortality. This information should reassure us that newly postmenopausal women who want to take hormone replacement therapy for symptom control can do so.
(LOE = 1a)

#### Reference

Salpeter SR, Walsh JME, Greyber E, Ormiston TM, Salpeter EE. Mortality associated with hormone replacement therapy in younger and older women. J Gen Intern Med 2004; 19:791-804.

#### Study Design

Meta-analysis (randomised controlled trials)

#### Setting

Outpatient (any)

#### Synopsis

This meta-analysis represents an attempt to look at the available data on hormone replacement therapy (HRT) in postmenopausal women to give some shading to the general (current) feeling that estrogens are 'bad'. The investigators identified, using several databases, all randomised studies of HRT in postmenopausal women, including the Women's Health Initiative Study published in 2002. They included studies that lasted at least six months and reported at least one death. This study was performed using appropriate meta-analytic techniques for choosing studies, extracting the data, and assessing validity. The authors combined the results from 30 studies enrolling more than 26 000 women. Overall total deaths, cardiovascular deaths, and cancer deaths were not different between the groups receiving HRT or placebo. However, after analysing separately by age, there was an overall survival benefit in women younger than 60 years (odds ratio = 0.61; 95% CI, 0.39–0.95). This benefit translates into a number needed to treat of 44 (95% CI, 29–88). Looking at outcomes individually, cardiovascular-related or cancer-related death rates were not affected by treatment. The benefit was not seen in women 60 years and older.

### Clinical question

Do antioxidants prevent gastrointestinal cancers?

#### Bottom line

Antioxidants do not prevent gastrointestinal cancers. In fact, in pooled results of high-quality studies, antioxidants increased overall mortality.
(LOE = 1a)

#### Reference

Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis. Lancet 2004; 364:1219-28.

### Study Design

Meta-analysis (randomised controlled trials)

### Setting

Various (meta-analysis)

### Synopsis

This is a Cochrane Review that follows their usual rigorous methods of searching, identification of unpublished data, and data extraction. The authors included all trials that randomised participants to supplementation with antioxidants (beta-carotene, vitamins A, C, and E, and selenium, as different combinations or separately) versus placebo, and that reported the incidence of gastrointestinal cancers. The authors assessed the methodological quality of trials and calculated whether the findings were consistent across trials. A total of 14 randomised controlled trials with 170 525 patients were evaluated. The number of patients in each trial ranged from 226 to nearly 40 000. Half the studies of cancer incidence were of good quality; seven of the nine that also reported mortality were of good quality. None of the supplements protected against esophageal cancer, gastric cancer, colorectal cancer, or pancreatic cancer. In the high-quality studies, antioxidants increased overall mortality (8.0% vs 6.6%). This translates to a number needed to treat to harm of 69 for one additional death (95% CI, 58–85). It is interesting to note that four trials of selenium (three with unclear or poor methodology) reduced the incidence of gastrointestinal cancer (odds ratio = 0.49; 95% CI, 0.36 - 0.67). Selenium should be evaluated in randomised trials with sound methods.

## Clinical question

Is a vaccine effective against human papillomavirus strains associated with cervical cancer?

### Bottom line

A bivalent vaccine against human papillomavirus (HPV) types 16 and 18 is well-tolerated and effective in reducing HPV infection and HPV-associated cytologic abnormalities. What we need now is a larger, longer-termed, adequately powered study to look at the effect of this vaccine on the development of cervical cancer.
(LOE = 1b)

### Reference

Harper DM, Franco EL, Wheeler C, et al. Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial. Lancet 2004; 364:1757-65.

### Study Design

Randomised controlled trial (double-blinded)

### Allocation

Concealed

### Setting

Population-based

### Synopsis

This team of researchers randomly assigned healthy women aged 15 to 25 years with no more than six sexual partners and no history of condyloma or cervical cancer to receive a bivalent vaccine active against HPV serotypes 16 and 18 or placebo. They administered the vaccine or placebo at 0, 1, and 6 months. They evaluated the patients after 27 months to determine the presence of HPV infection or cytologic abnormalities. Using an intention-to-treat approach to these outcomes, the vaccine was 95% effective against persistent HPV infection and 93% effective against cytologic abnormalities associated with HPV. In the intention-to-treat analysis, the absolute reduction in new HPV infections was 6.4% (number needed to treat [NNT] = 16) and 3.5% for persistent infections (NNT= 29). Other than local injection site symptoms, there were no differences in side effects between the active and placebo vaccines.