# POEMs

## *Patient-Oriented Evidence That Matters*

### *H. pylori* Eradication: Effective for Cure or Improvement of Functional Dyspepsia, Especially if Eradication Is Confirmed

#### Clinical Question

How effective is the eradication of *Helicobacter pylori* for the treatment of functional dyspepsia?

#### Bottom Line

*H. pylori* eradication is an effective treatment for cure or improvement of functional dyspepsia symptoms, especially if there is evidence of successful *H. pylori* eradication. (Level of Evidence = 1a)

#### Synopsis

The systematic review updated a previous Cochrane review with 10 new trials and 2,896 patients, for a total of 29 trials and 6,781 patients. The authors did a high-quality systematic review to identify randomized trials with at least three months of follow-up, using a random effects meta-analysis. Only six studies were classified as having a low risk of bias, and the most common problems were unclear allocation concealment and unclear complete outcome reporting. Based on 18 studies with 4,564 patients, *H. pylori* eradication therapy decreased the likelihood of failure to cure functional dyspepsia (relative risk [RR] = 0.91; 95% CI, 0.88 to 0.94; $I^2$ = 7%; number needed to treat [NNT] = 14). There was some evidence for publication bias, suggesting that smaller, negative trials were not published. The benefit was consistent regardless of the comparator (i.e., placebo or antisecretory therapy) or study quality. Based on 22 studies with 5,193 patients, *H. pylori* eradication therapy decreased the likelihood of failure to improve symptoms, without evidence of publication bias but with moderate heterogeneity (RR = 0.84; 95% CI, 0.78 to 0.91; $I^2$ = 69%; NNT = 9). Sixteen studies reported whether eradication was successful, and patients with successful eradication were significantly less likely to fail to improve or fail to be cured than those who received the comparator (RR = 0.74; 95% CI, 0.64 to 0.85; $I^2$ = 82%; NNT = 6). There was significant heterogeneity, and funnel plot asymmetry suggests possible publication bias.

**Study design:** Meta-analysis (randomized controlled trials)

**Funding source:** Self-funded or unfunded

**Setting:** Outpatient (any)

**Reference:** *Ford AC, Tsipotis E, Yuan Y, et al. Efficacy of* Helicobacter pylori *eradication therapy for functional dyspepsia: updated systematic review and meta-analysis.* Gut. *2022;71(10):1967-1975.*

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### Mindfulness-Based Stress Reduction Is Noninferior to Escitalopram for Adults With Anxiety Disorder

#### Clinical Question

Is mindfulness-based stress reduction noninferior to escitalopram for the treatment of anxiety disorders in adults?

#### Bottom Line

The study findings show that standard mindfulness-based stress reduction is noninferior to pharmacotherapy with escitalopram for the treatment of anxiety disorders in adults. The primary outcome measurement occurred at eight weeks from baseline. At six months, the anxiety scores remained improved despite only 52% of the escitalopram group and 28% of the mindfulness-based stress reduction group continuing their treatments. (Level of Evidence = 1b)

#### Synopsis

Mindfulness-based stress reduction is effective for decreasing anxiety symptoms in adults. It remains unclear how effective this technique is compared with standard pharmacotherapy. The investigators identified adults 18 to 75 years of age with a primary diagnosis of generalized anxiety disorder, social anxiety disorder, panic disorder, or agoraphobia. Eligible patients (N = 276) randomly received assignment (concealed allocation) to mindfulness-based stress reduction training (an eight-week protocol with weekly 2.5-hour-long classes, a daylong weekend retreat class, and 45-minute daily home practice exercises) or escitalopram (10 mg orally

per day; increased to 20 mg per day at week 2, if tolerated). Individuals masked to treatment group assignment assessed symptom severity using a standard validated anxiety scoring tool. Follow-up occurred at eight weeks for 95% of participants.

Using intention-to-treat and per-protocol analyses at the primary endpoint of eight weeks, mindfulness-based stress reduction therapy met the criteria for noninferiority compared with escitalopram. At six months of follow-up, 52% of patients were still taking escitalopram, whereas only 28% of patients were still doing regular mindfulness meditation, but the anxiety scores remained improved.

**Study design:** Randomized controlled trial (single-blinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Outpatient (any)

**Reference:** *Hoge EA, Bui E, Mete M, et al. Mindfulness-based stress reduction vs escitalopram for the treatment of adults with anxiety disorders: a randomized clinical trial.* JAMA Psychiatry. *2023;80(1):13-21.*

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## Twice-Daily Low-Dose Aspirin Is Similar to Enoxaparin for Thromboprophylaxis After Inpatient Treatment for Fracture

### Clinical Question

Is twice-daily low-dose aspirin noninferior to enoxaparin, a low-molecular-weight heparin, for thromboprophylaxis after an extremity, acetabular, or pelvic fracture?

### Bottom Line

Aspirin is noninferior to enoxaparin for thromboprophylaxis following inpatient treatment of a fracture. It is more affordable and convenient and preferred by patients. (Level of Evidence = 1b)

### Synopsis

The large pragmatic trial included 12,211 adults with an extremity fracture treated operatively, or a pelvic or acetabular fracture treated with or without surgery. The patients were randomized to receive aspirin, 81 mg twice daily, or enoxaparin, 30 mg twice daily. The patients received the assigned medication while in the hospital and then followed their hospital's postdischarge thromboprophylaxis protocol. Patients with fractures of the hands or feet, who had already received three or more doses of thromboprophylaxis, or those admitted more than 48 hours after the injury were excluded. Patients taking an anticoagulant on admission or who had a venous thromboembolism in the past three months were also excluded. At baseline, the mean age of participants was 45 years, 62% were men, and 20% were Black. The most common site of injury was the lower extremity, and 67% of patients had only a lower extremity fracture. Groups were balanced at the start of the study, and analysis was by intention to treat. The primary outcome of 90-day all-cause mortality occurred in 0.78% of patients in the aspirin group and 0.73% in the enoxaparin group (95% CI for the difference, −0.27 to 0.38). There was no difference in the likelihood of any pulmonary embolism (1.49% in each group), but there was an increase in deep venous thromboses in the aspirin group (2.51% vs. 1.71%; 95% CI for difference, 0.28 to 1.31; number needed to harm = 125), although most of the increase was in distal clots. There was no difference in the rate of bleeding complications, infections, or wound complications.

**Study design:** Randomized controlled trial (single-blinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Inpatient (any location)

**Reference:** *O'Toole RV, Stein DM, O'Hara NN, et al.; Major Extremity Trauma Research Consortium (METRC). Aspirin or low-molecular-weight heparin for thromboprophylaxis after a fracture.* N Engl J Med. *2023;388(3):203-213.*

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## Morning and Bedtime Dosing of Antihypertensives Have Similar Rates of Major Cardiovascular Events

### Clinical Question

Does bedtime administration of blood pressure medications improve outcomes?

### Bottom Line

In contrast with the large Hygia Chronotherapy Trial, this equally large TIME (Treatment in Morning versus Evening) study found that it

does not matter when patients take their blood pressure medications. Patients should take their antihypertensive medication when it is best for them. (Level of Evidence = 2b)

## Synopsis

The Hygia Chronotherapy Trial included more than 19,000 adults with hypertension and found that bedtime administration of antihypertensive medications decreased cardiovascular death and morbidity over more than six years of follow-up. However, hypertension researchers thought the results were too good to be true. An independent review of the data confirmed the original study's findings. In the TIME study, researchers randomly assigned adults with treated hypertension to take all their antihypertension medications in the morning (6 a.m. to 10 a.m.; n = 10,601) or in the evening (8 p.m. to midnight; n = 10,503). The researchers instructed the evening-dose patients who were taking a diuretic to take the diuretic earlier (6 p.m.) if they were troubled by nocturia, or in the morning if the nocturia continued. The researchers used intention-to-treat analysis to compare the rate of the primary outcome: a composite of vascular death or hospitalization for nonfatal myocardial infarction or nonfatal stroke. The researchers used patient-submitted data supplemented with data from national registries. Adjudicators masked to allocation made the final outcome determinations. A total of 90.5% of participants were White, 42.5% were women, and 12.9% had preexisting cardiovascular disease. The mean baseline characteristics of each group were balanced. After a median follow-up of 5.2 years, 3.7% of the morning-dose patients and 3.4% of the evening-dose patients experienced the endpoint, and their time to first occurrence was similar. There was no difference in the rate of any of the individual outcome components or in all-cause mortality (4.1% vs. 4.2%, respectively). The rate of adverse effects, including excessive bathroom visits (day or night; 36.4% vs. 40.0%, respectively), were similar for both groups.

**Study design:** Randomized controlled trial (single-blinded)

**Funding source:** Government

**Allocation:** Concealed

**Setting:** Outpatient (any)

**Reference:** *Mackenzie IS, Rogers A, Poulter NR, et al.; TIME Study Group. Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study): a prospective, randomised, open-label, blinded-endpoint clinical trial.* Lancet. *2022; 400(10361):1417-1425.*

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**Editor's Note:** Dr. Ebell is deputy editor for evidence-based medicine for *AFP* and cofounder and editor-in-chief of Essential Evidence Plus, published by Wiley-Blackwell. ■