POEMs

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This series is coordinated by Sumi Sexton, MD, Associate Deputy Editor.

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Chondroitin/Glucosamine Equal to Celecoxib for Knee Osteoarthritis

Clinical Question

Is combined chondroitin/glucosamine as effective as celecoxib (Celebrex) in reducing pain and improving function in patients with painful knee osteoarthritis?

Bottom Line

For patients with painful knee osteoarthritis, a high-dose combination of glucosamine hydrochloride (1,500 mg) and chondroitin (1,200 mg) was as effective in lessening pain and stiffness and improving function as celecoxib (200 mg). Other studies have not found benefit. It is time for someone to analyze all the studies of chondroitin/glucosamine to determine who is most likely to benefit. (Level of Evidence = 1b)

Synopsis

The 606 patients in this study were enrolled by one of 42 rheumatologists practicing in France, Germany, Poland, or Spain. The patients were an average age of 63 years, most were women (84%), and almost all were white (99%). They all had radiographic evidence of knee osteoarthritis and had severe pain as measured by a score greater than 300 (of a possible 500) on the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index, which is the standard research scale used to evaluate pain, stiffness, and function. The patients were randomized (concealed allocation unknown) to receive 400-mg chondroitin sulfate/500-mg glucosamine hydrochloride three times a day or 200-mg celecoxib every day for six months (both with matched placebo). The glucosamine/chondroitin dose is a little higher than is typically recommended and studied. At six months, using a modified intention-to-treat analysis that included only 94% of enrolled patients, WOMAC pain scores were decreased by 50% in both groups, stiffness scores decreased 46.9% with the combination vs. 49.2% with celecoxib (P = not significant), and function improved similarly (decreased in 45.5% vs. 46.4%; P = not significant).

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Uncertain

Setting: Outpatient (specialty)

Reference: *Hochberg MC, Martel-Pelletier J, Monfort J, et al.; MOVES Investigation Group. Combined chondroitin sulfate and glucosamine for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib.* Ann Rheum Dis. *2016;75(1):37-44.*

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Colorectal Cancer Screening Modalities: Variable Uptake, Variable Yield

Clinical Question

How acceptable are various colorectal cancer screening modalities, and what is the yield in population-based screening programs?

Bottom Line

Based on the initial round of screening in this randomized trial, it appears that more patients complete fecal immunochemical testing (FIT) than colonography or colonoscopy. Using the most conservative estimate, the yields of advanced adenomas and ▶

advanced neoplasms are similar. If considering only those participants who were actually screened (not the total number invited to participate), colonoscopy found more of these lesions but also had the lowest participation rate. (Level of Evidence = 2b)

Synopsis

These researchers assigned 16,087 patients to one of four screening approaches: three cycles of FIT every two years (n = 9,739), a single reduced-preparation computed tomographic colonography (n = 2,617), a single full-preparation computed tomographic colonography (n = 2,625), or a single colonoscopy (n = 1,106). The participants were all residents of a single region in Italy, were between 55 and 64 years of age, and had not had recent colorectal cancer screening. If a FIT result or any of the colonography results were abnormal, the patients were invited to have colonoscopy. One of two experienced pathologists evaluated all the colorectal lesions; the paper does not report if they were aware of allocation. The researchers classified lesions as follows: hyperplastic polyp; or serrated, tubular, tubulovillous, or villous adenoma or adenocarcinoma. Additionally, they defined advanced adenoma as being greater than 9 mm or with more than 20% villous histologic component or with severe dysplasia (or any combination of these). They also defined advanced neoplasia as cancer or advanced adenoma. Finally, to avoid differential participation in the program, spouses were clustered to the same screening modality.

This paper presents data from the first screening round. Slightly more than one-half of the patients were women and slightly less than one-half were of low socioeconomic status; the average age was 59 years. Among the invitees, one-half completed the first round of FIT, approximately 25% completed each of the two colonography modalities, and approximately 12% completed the colonoscopy. Keep in mind that the FIT group still has two more cycles to complete, so the participation rate for the whole study is likely to be much lower. The findings depended on the denominator. First, regardless of denominator, they found only 20 cancers. If you look at everyone who was invited, approximately 1% of the time the modalities detected advanced adenomas and advanced neoplasms. Among the 6,116 participants who were actually screened, however, the numbers look different. FIT identified advanced adenomas and advanced neoplasms slightly less than 2% of the time, whereas the various colonographies found them approximately 5% of the time and colonoscopy 7% of the time. A downside to colonography is the age-old bane of clinicians: 5% of the time, radiologists identified extracolonic findings outside the area of interest that were of uncertain importance and were likely to boost the cost without improving outcomes.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Uncertain

Setting: Population-based

Reference: *Sali L, Mascalchi M, Falchini M, et al.; SAVE study investigators. Reduced and full-preparation CT colonography, fecal immunochemical test, and colonoscopy for population screening of colorectal cancer: a randomized trial.* J Natl Cancer Inst. *2015;108(2):djv319.*

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Meta-Analysis: Intensive BP Control Decreases Major CV Events and Stroke, but Not MI, Heart Failure, or Mortality

Clinical Question

Does intensive lowering of blood pressure (BP) improve the lives of patients with hypertension?

Bottom Line

Patients with hypertension who are treated intensively are less likely to have major cardiovascular (CV) events, stroke, or progression of albuminuria or retinopathy than those treated less intensively, but intensive lowering had no meaningful effect on myocardial infarctions (MIs), heart failure, or mortality. (Level of Evidence = 1a)

Synopsis

This team of researchers reviewed several databases and registries to identify randomized trials that lasted at least six months and that compared more intensive vs. less intensive BP lowering in patients with hypertension. Two authors independently determined which studies to include and assessed the included studies' methodologic quality. They were interested in a range of clinically meaningful outcomes (e.g., mortality) as well as irrelevant outcomes (e.g., progression of albuminuria), singly or as a composite. Ultimately, they included 21 reports from 19 trials with nearly 45,000 patients followed for an average of four years. Approximately one-half of the studies were of modest to poor quality.

The intensive treatment group had mean BP levels of 133/76 mm Hg compared with 140/81 mm Hg in the less-intensive group. The data show small reductions in the rate of major CV events (5.7% vs. 5.8%; number needed to treat [NNT] = 838) and stroke (2.4% vs. 2.6%; NNT = 406), but no significant reduction in the rate of

MIs (2%). Although there were decreases in the rates of albuminuria progression and retinopathy progression, there were no significant decreases in the rates of heart failure, end-stage kidney disease, overall mortality, or CV mortality. Most studies failed to report on the harms of intensive BP lowering. In the six studies that did, serious harms occurred in 1.2% per year in the intensive group vs. 0.9% per year in the nonintensive group, with severe hypotension occurring in 0.3% per year vs. 0.1%. Finally, patients with preexisting diabetes mellitus, renal disease, or vascular disease treated more intensively generally had better outcomes than those treated less intensively.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Outpatient (any)

Reference: *Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis.* Lancet. *2016;387(10017):435-443.*

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Behavioral Interventions Reduce Inappropriate Antibiotic Prescribing for Acute Respiratory Tract Infections

Clinical Question

Do behavioral interventions reduce rates of inappropriate antibiotic prescribing for acute respiratory tract infections in primary care?

Bottom Line

Requiring clinicians to justify antibiotic prescribing in the permanent electronic health record and to undergo periodic peer comparisons of prescribing rates are effective interventions for reducing inappropriate antibiotic prescribing for acute respiratory tract infections. Helpful reminders and suggested treatment alternatives do not reduce inappropriate prescribing rates. Information alone rarely changes behavior, but the desire to conform with our peers can be very persuasive. (Level of Evidence = 1b–)

Synopsis

Clinical guidelines encourage avoiding antibiotics for infections when treatment is of minimal, if any, benefit. However, inappropriate antibiotic prescribing for acute respiratory tract infections persists. These investigators invited 49 practices in Massachusetts and California (N = 243 clinicians) to receive various combinations of behavioral interventions aimed at reducing inappropriate antibiotic prescribing. The first intervention used automated alternative treatment suggestions when clinicians attempted to prescribe antibiotics for antibiotic-inappropriate diagnoses. A second intervention required clinicians to enter an antibiotic justification note that became a permanent part of the medical record. The third intervention distributed periodic e-mails to participating clinicians labeling them as either a "top performer" or "not a top performer" by comparing their antibiotic prescribing behavior with that of their peers.

Clinicians included internists (60%), nurse practitioners/physician assistants (19%), and family physicians (13%). The study excluded patients with chronic medical conditions that necessitate more frequent antibiotic prescriptions for acute respiratory tract infections (e.g., emphysema). Practices were randomized to receive zero, one, two, or all three interventions for 18 months, and no cases were lost to follow-up. Not surprisingly, the control group significantly decreased inappropriate antibiotic prescribing rates (11% absolute reduction) during the study period. This is known as the Hawthorne effect: changing your behavior because you know you are being observed. Both the accountable justification and peer comparison interventions significantly decreased antibiotic prescribing rates compared with the control group (–7.0% and –5.2%, respectively). However, the suggested alternatives intervention did not significantly reduce antibiotic prescribing rates compared with control. The latter result is disheartening but consistent with previous findings about influencing clinical decision making: Information alone rarely changes behavior. The most powerful influence continues to be peer pressure and the desire to conform.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Uncertain

Setting: Outpatient (primary care)

Reference: *Meeker D, Linder JA, Fox CR, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial.* JAMA. *2016;315(6):562-570.*

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