

CONTENTS **Annals of Internal Medicine**

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ARTICLES

Tiotropium in Combination with Placebo, Salmeterol, or Fluticasone–Salmeterol for Treatment of Chronic Obstructive Pulmonary Disease. A Randomized Trial 545

S.D. Aaron, K.L. Vandemheen, D. Fergusson, F. Maltais, J. Bourbeau, R. Goldstein, M. Balter, D. O'Donnell, A. McIvor, S. Sharma, G. Bishop, J. Anthony, R. Cowie, S. Field, A. Hirsch, P. Hernandez, R. Rivington, J. Road, V. Hoffstein, R. Hodder, D. Marciniuk, D. McCormack, G. Fox, G. Cox, H.B. Prins, G. Ford, D. Bleskie, S. Doucette, I. Mayers, K. Chapman, N. Zamel, and M. FitzGerald, for the Canadian Thoracic Society/Canadian Respiratory Clinical Research Consortium
Scant evidence supports prescribing combinations of inhaled corticosteroids and long-acting β -agonists and anticholinergic bronchodilators for chronic obstructive pulmonary disease (COPD). Investigators randomly assigned 449 adults with moderate or severe COPD to receive tiotropium with placebo, with salmeterol, or with fluticasone–salmeterol for 1 year. The exacerbation rates for the 3 groups were 63%, 65%, and 60%, respectively. Compared with tiotropium alone, 3-drug therapy but not 2-drug therapy had fewer exacerbations requiring hospitalization.

Summary for Patients I-12

Sequential Therapy versus Standard Triple-Drug Therapy for *Helicobacter pylori* Eradication. A Randomized Trial 556

D. Vaira, A. Zullo, N. Vakil, L. Gatta, C. Ricci, F. Perna, C. Hassan, V. Bernabucci, A. Tampieri, and S. Morini
Eradication rates of *Helicobacter pylori* infection are decreasing worldwide because of increasing resistance to antimicrobials. In this double-blind trial, 300 adults with dyspepsia or peptic ulcers were randomly assigned to a 10-day sequential regimen (pantoprazole, amoxicillin, and placebo taken for 5 days followed by pantoprazole, clarithromycin, and tinidazole taken for 5 days) or standard 10-day therapy (pantoprazole, clarithromycin, and amoxicillin). The eradication rate was higher with the sequential regimen than with standard therapy, especially in patients with clarithromycin-resistant strains. The incidence of side effects did not differ between groups.

Summary for Patients I-20

Adherence to Nonnucleoside Reverse Transcriptase Inhibitor–Based HIV Therapy and Virologic Outcomes 564

J.B. Nachega, M. Hislop, D.W. Dowdy, R.E. Chaisson, L. Regensberg, and G. Maartens
Protease-based HIV treatment regimens require 95% or higher adherence to achieve optimal viral load suppression. Nachega

and colleagues asked whether regimens based on nonnucleoside reverse transcriptase inhibitors (NNRTIs) require the same high level of adherence. They reviewed pharmacy claim records and virologic responses in 2821 HIV-infected adults enrolled in an HIV/AIDS disease management program in South Africa. After a 2.2-year follow-up, 25% of patients who had 50% to 60% adherence achieved viral load suppression, a rate that increased linearly to 73% of those who had 90% to 100% adherence with NNRTI–based therapy. Better adherence increases the chance of success, but the requirement for adherence appears less stringent than that of regimens that do not contain NNRTIs.

Summary for Patients I-28

Brief Communication: Treatment of *Enterococcus faecalis* Endocarditis with Ampicillin plus Ceftriaxone 574

J. Gavaldà, O. Len, J.M. Miró, P. Muñoz, M. Montejo, A. Alarcón, J. de la Torre-Cisneros, C. Peña, X. Martínez-Lacasa, C. Sarria, G. Bou, J.M. Aguado, E. Navas, J. Romeu, F. Marco, C. Torres, P. Tornos, A. Planes, V. Falcó, B. Almirante, and A. Pahissa
A 4- to 6-week course of penicillin or ampicillin plus an aminoglycoside is currently recommended for treating enterococcal endocarditis. However, this regimen is ineffective against *Enterococcus faecalis* organisms with high-level aminoglycoside resistance (HLAR). Gavaldà and colleagues evaluated the efficacy and safety of ampicillin plus ceftriaxone for treating *E. faecalis* endocarditis in patients who could not tolerate aminoglycosides because of nephrotoxicity. Twenty-one patients had HLAR organisms and 22 patients did not. A 6-week course effectively treated both groups.

Summary for Patients I-56

REVIEWS

Meta-analysis: Chondroitin for Osteoarthritis of the Knee or Hip 580

S. Reichenbach, R. Sterchi, M. Scherer, S. Trelle, E. Bürgi, U. Bürgi, P.A. Dieppe, and P. Jüni
Many physicians use oral chondroitin, a highly hydrophilic, gel-forming polysaccharide macromolecule, to treat osteoarthritis. Meta-analyses of clinical trials have described moderate to large benefits of chondroitin, but recent large-scale trials did not find evidence of an effect. Reichenbach and colleagues performed a systematic review of randomized, controlled trials to determine the effect of chondroitin on pain and joint space width. They found little or no symptomatic benefit of chondroitin in the recent high-quality large-scale trials, and they discourage using chondroitin in routine clinical practice.

Continued on page I-6

Narrative Review: Antiretroviral Therapy to Prevent the Sexual Transmission of HIV-1 591

M.S. Cohen, C. Gay, A.D.M. Kashuba, S. Blower, and L. Paxton

Antiretroviral therapy (ART) has prolonged and improved the lives of persons with HIV infection. Cohen and colleagues reviewed relevant publications on the use of ART to prevent the sexual transmission of HIV and discuss 3 ways that ART can prevent sexual transmission of HIV: 1) effective treatment of HIV-infected persons to reduce transmission to sexual partners, 2) nonoccupational postexposure prophylaxis, and 3) preexposure prophylaxis.

PERSPECTIVE

Linking Cost Sharing to Value: An Unrivalled Yet Unrealized Public Health Opportunity 602

R.S. Braithwaite and A.B. Rosen

The rationale for cost sharing is often a moral hazard argument—that individuals may overuse care if they do not share its costs. In practice, people apply the concept of cost sharing without taking into account the clinical value of the service. Cost sharing could be harmful if it discouraged patients from using high-value services. The authors distinguish between appropriate (low ratio of benefits to costs) and inappropriate (high ratio of benefits to costs) settings for cost sharing and discuss how cost-effectiveness analysis can help policymakers to decide when cost-sharing policies are appropriate. Systematic efforts to discourage inappropriate cost sharing may improve public health.

EDITORIALS

Optimal Treatment of Chronic Obstructive Pulmonary Disease: The Search for the Magic Combination of Inhaled Bronchodilators and Corticosteroids 606

G.J. Criner

In this issue, Aaron and colleagues performed a randomized trial in which all patients with moderate to severe COPD received tiotropium with random assignment to placebo, a long-acting inhaled bronchodilator (salmeterol), or a combination of inhaled corticosteroid (fluticasone) and salmeterol. The primary outcome, the total exacerbation rate, was the same in all 3 groups. Relative to tiotropium alone, tiotropium plus fluticasone-salmeterol benefited several secondary outcomes: severe exacerbations that required hospitalization, lung function, and quality of life. Studies such as this suggest that we may finally be on the threshold of therapies that decrease the morbidity and mortality of COPD.

Hungering for HAART 609

J.S.G. Montaner and R.S. Hogg

Expansion of highly active antiretroviral therapy (HAART) programs in South Africa and other low- and medium-

income nations should remain a top priority. In this issue, Nachegea and colleagues used pharmacy refill or claim data to measure adherence to nonnucleoside reverse transcriptase inhibitor-based HAART in patients in a private-sector, publicly sponsored HIV/AIDS program in South Africa. Increasing adherence was associated with an increase in the probability of sustained virologic suppression at all levels of adherence beyond 50%. The authors' approach to measuring adherence could become an important tool to evaluate the effectiveness of public-sector programs in low- and medium-income nations.

Chondroitin for Pain in Osteoarthritis 611

D.T. Felson

In this issue, Reichenbach and colleagues studied the 20 trials that have compared chondroitin with placebo or no treatment for pain in osteoarthritis of the hip or knee. The results varied widely. The best current evidence, from 3 large high-quality trials, states that chondroitin sulfate does not reduce joint pain in osteoarthritis. Nevertheless, some patients are convinced that it helps. Since frequent or severe adverse effects have not been reported, a trial of chondroitin sulfate may be worthwhile.

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Posttraumatic Stress Disorder Needs to Be Recognized in Primary Care 617

J. Fisher Wilson

Cover photograph by Morry Moskovitz, MD

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