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Delayed Prescription Strategies Decrease Antibiotic Use

Clinical Question

Is a method of delayed prescriptions for respiratory tract infections effective for decreasing antibiotic use?

Bottom Line

A delayed prescription approach in children and adults with acute respiratory tract infections, combined with explicit instructions for symptom control, is effective in decreasing antibiotic use, while not adversely affecting patient satisfaction or symptom duration or severity. Asking patients to call, pick up, or simply hold a prescription for a prescribed time resulted in fewer than 40% of patients receiving antibiotics. (Level of Evidence = 1b)

Synopsis

Primary care clinicians in 25 practices in the United Kingdom participated in this study. They enrolled 566 children (at least three years of age) and adults with acute respiratory infection evaluated for respiratory tract symptoms deemed to not require antibiotic treatment (62.5% of eligible visits). The patients were randomly assigned, using concealed allocation, to one of five strategies: (1) no prescription, (2) recontact the office if symptoms persist, (3) a postdated prescription was given, (4) a prescription was left at reception to be picked up if symptoms persisted, or (5) patients were given a prescription and asked not to fill it unless symptoms

persisted. The advice for length of delay was tailored to the type of illness (e.g., three days for ear infections, 10 days for acute cough). In addition, patients were also randomized to receive different advice for symptom control (type of analgesic or use of steam inhalation).

Symptom severity on the second and fourth days following the visit were similar between the no-prescription group and any of the delayed-prescription groups, as well as between these groups and the patients immediately treated with antibiotics. Patient satisfaction with the visit was also similar among all groups. The actual percentage of patients in the no-prescription or delayed-prescription groups that eventually took antibiotics ranged from 26% to 39% (difference not significant). Follow-up visits and complications were similar across all groups.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: Little P, Moore M, Kelly J, et al.; PIPS Investigators. Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomised controlled trial. *BMJ*. 2014;348:g1606.

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New Anticoagulants vs. Warfarin in Atrial Fibrillation: No Clear Winner

Clinical Question

Are the newer anticoagulants safer or more effective than warfarin (Coumadin) in patients with atrial fibrillation?

Bottom Line

In this meta-analysis, newer anticoagulants appear to be slightly more effective than warfarin in the short term (two years) in preventing strokes of all kinds in patients with atrial fibrillation. However, they are

no more effective than warfarin in preventing ischemic strokes, and they cause more gastrointestinal hemorrhage. The short-term nature of the included studies and a significant concern about publication bias suggests that the newer agents are by no means a slam dunk over warfarin. Because the patients taking warfarin only spent two-thirds of their time in therapeutic range, perhaps efforts to improve performance may be a wiser use of resources. (Level of Evidence = 1a-)

Synopsis

The authors of this study and the editors of *The Lancet* did a fairly abysmal job in communicating how this study was conducted. The abstract claims the authors searched a single database to identify phase-randomized trials comparing newer anticoagulants with warfarin in patients with atrial fibrillation. However, the methods section reports the authors conducted a prespecified analysis of four studies and does not describe a thing

about the search strategy. Additionally, the authors do not include data on ximelagatran, which was pulled because of safety concerns.

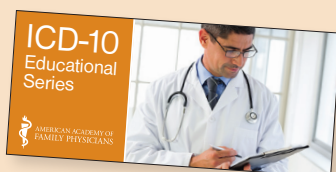
The authors pooled the data for nearly 72,000 patients with atrial fibrillation who received one of the newer anticoagulants (dabigatran [Pradaxa], rivaroxaban [Xarelto], apixaban [Eliquis], or edoxaban; n = 42,411) or warfarin (n = 29,272). The authors evaluated the outcomes by intention to treat when possible, but made no adjustments for performing multiple analyses. Two of the four trials included nearly one-third of the patients with CHADS₂ (congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, and stroke or transient ischemic attack) scores of 0 to 1, which is a group that may not need anticoagulation. Overall, approximately one-fourth of the patients had paroxysmal atrial fibrillation. The median duration of follow-up was 2.2 years, and the warfarin-treated patients were in therapeutic range only two-thirds of the time. ►

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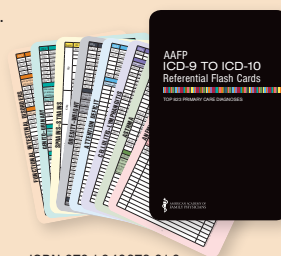
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Patients receiving the newer agents had a lower risk of stroke or systemic embolic events than patients taking warfarin (3.1% vs. 3.8%; relative risk = 0.81; number needed to treat [NNT] = 148; 95% confidence interval [CI], 103 to 261). There were no statistically significant differences in the rate of ischemic stroke or myocardial infarction. Patients taking the newer agents had fewer hemorrhagic strokes (0.4% vs. 0.9%; NNT = 220; 95% CI, 170 to 308) and intracranial hemorrhages (0.7% vs. 1.4%; NNT = 132; 95% CI, 108 to 169). Furthermore, all-cause mortality was slightly lower in patients receiving the newer agents (6.9% vs. 7.7%; NNT = 129; 95% CI, 84 to 279). However, patients taking newer agents had more gastrointestinal bleeding (2.6% vs. 2%; number needed to treat to harm = 185; 95% CI, 128 to 335). Although the study was unfunded, the authors had heavy ties to industry, which may explain their sloppiness in describing their methods. For example, they do not even try to evaluate the potential for publication bias, an issue especially important because industry-sponsored studies have a long track record of not finding their way to publication.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet*. 2014;383(9921):955-962.

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One in Five Patients Overdiagnosed with Lung Cancer Screening

Clinical Question

In patients found to have lung cancer by screening, what is the likelihood that the identified cancer would never have affected that patient?

Bottom Line

In patients screened for lung cancer using low-dose computed tomography (LDCT),

more than 18% of all lung cancers found are slow-growing and will not cause symptoms or harm during an average 6.4 years of follow-up. This risk of overdiagnosis should be part of the discussion regarding whether to screen. (Level of Evidence = 1b)

Synopsis

Early detection of disease via screening usually makes sense, unless that earlier detection leads to identification of a disease that is never destined to cause problems in the patient. We cannot pinpoint which patients are overdiagnosed; all we can do is understand the concept that some patients will be identified and treated for a disease that would never have become clinically apparent. This study is an analysis of the previously reported National Lung Screening Trial using extended follow-up data. This study enrolled 53,452 patients at high risk of lung cancer (i.e., those between 55 and 74 years of age with at least a 30 pack-year history of smoking). Patients were randomized to receive three annual screens with LDCT or single-view posterior-anterior chest radiography. Patients were followed up for an average of 6.4 years. More lung cancers were reported in the LDCT arm of the study (1,089) than in the chest radiography arm (969). The excess number of cancers in the LDCT arm (18.5%; 95% confidence interval, 5.4% to 30.6%) represents the total number of cancers that would not have become clinically apparent during the screening period had screening not been performed. Most (78.9%) of the bronchioalveolar lung cancers found were an overdiagnosis, and 22.5% of non-small cell lung cancers found were an overdiagnosis.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Uncertain

Setting: Outpatient (any)

Reference: Patz EF Jr, Pinsky P, Gatsonis C, et al.; NLST Overdiagnosis Manuscript Writing Team. Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA Intern Med*. 2014; 174(2):269-274.

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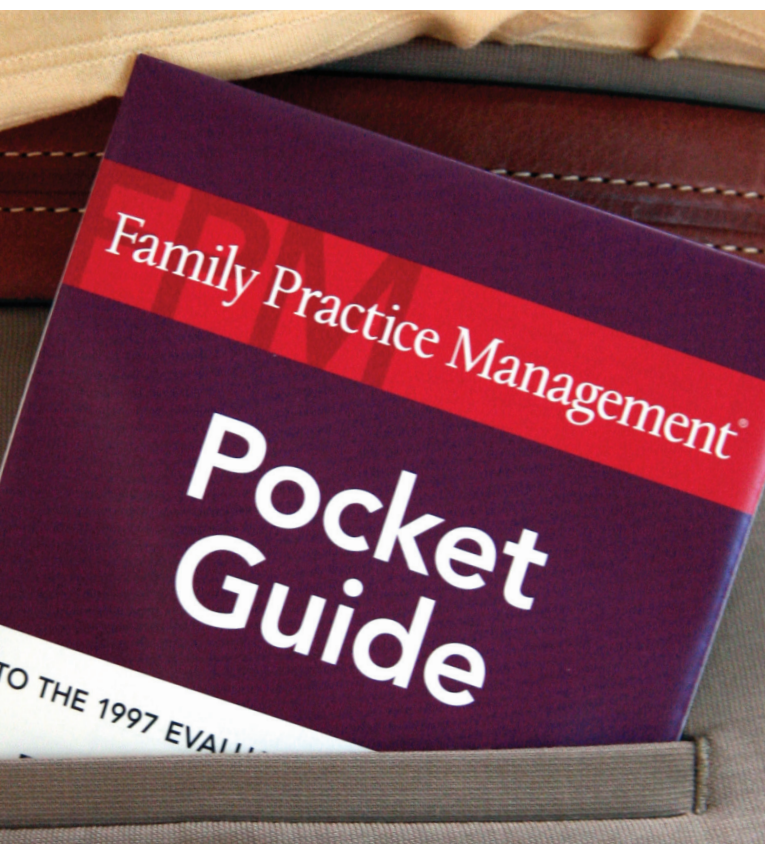
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POEMs

Stable TSH Can Be Rechecked in Two Years

Clinical Question

How much do seemingly stable thyroid tests vary over time?

Bottom Line

Most patients receiving thyroid replacement therapy with less than 125 mcg of levothyroxine per day can wait two years before monitoring thyroid-stimulating hormone (TSH) levels if their results are normal. Fewer than one in 10 patients who take less than 125 mcg of levothyroxine per day with a normal TSH level will have an abnormal laboratory value one year later. The likelihood goes up to 26.7% if the dosage is higher than 125 mcg of levothyroxine per day. Patients with TSH levels closer to the upper or lower limits of normal will also be slightly more likely to have an abnormal value in one year. (Level of Evidence = 1b)

Synopsis

These authors identified 715 patients (84% women; average age = 54 years) in a single primary care practice who were treated for hypothyroidism and had a normal TSH value (0.3 to 5.0 mIU per L). They recorded all subsequent TSH levels in these patients for the following six years. Age, sex, body mass index, and history of chronic autoimmune thyroiditis were not associated with the development of a subsequent abnormal TSH level, but the dosage of levothyroxine was associated. Approximately one in four patients taking more than 125 mcg of levothyroxine per day (26.7%) had an abnormal TSH level one year later. Most of the patients taking lower dosages (91.1%) had normal TSH levels one year later.

Study design: Cohort (retrospective)

Funding source: Self-funded or unfunded

Setting: Outpatient (primary care)

Reference: Pecina J, Garrison GM, Bernard ME. Levothyroxine dosage is associated with stability of thyroid-stimulating hormone values. *Am J Med.* 2014;127(3):240-245.

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