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Patient Oriented Evidence that Matters

False-positive PSA associated with increased worry and fears

McNaughton-Collins M, Fowler FJ, Caubet JF, et al. Psychological effects of a suspicious prostate cancer screening test followed by a benign biopsy result. Am J Med 2004; 117:719–725.

Clinical Question

Do men who receive a false-positive prostate specific antigen (PSA) test result worry more about prostate cancer than men who receive a negative result?

Bottom Line

False-positive results of screening tests are not benign; they have a psychological cost. Men who received false-positive PSA test results reported having thought and worried more about prostate cancer despite receiving a negative follow-up (prostate biopsy) result. They also think that the false-positive result makes them more likely to develop prostate cancer. Screening can be bad for our patients' mental health. (Level of evidence [LOE]=**1b**)

Study Design

Cohort (prospective)

Setting

Outpatient (primary care)

Synopsis

The investigators identified 167 men from a group of consecutive men who had a negative biopsy following a suspicious PSA test. In other words, these men had a false-positive PSA result. For comparison, they also identified 233 men who had a normal PSA result. The men were mailed a brief questionnaire approximately 6 weeks after their biopsy or normal PSA test result.

Overall, 85% of the men responded by returning the survey, which is a very good response for a survey. Of the men who had a false-positive result, 49% reported having thought about prostate cancer either "a lot" or "some of the time" compared with 18% of the control patients ($P<.001$). As compared with 8% in the control group, 40% of the men in the false-positive group also worried "a lot" (7%) or "some of the time" (33%) about the possibility of developing prostate cancer. The false-positive group did not worry more than the control group about dying soon. Sixty-two percent of the men with a negative biopsy reported being "a lot" reassured by the result, despite the 10% false-negative rate associated with biopsy.

As with women who receive a false-positive mammogram result, instead of being angry at the erroneous test result, men with a false-positive PSA felt they "dodged a bullet": significantly more men in this group reported their lives changed for the better (31% vs 13%; $P<.001$). And, also similar to women experiencing a false-positive mammogram, the men in the false-positive group were more likely to think their chance of getting prostate cancer was "much more" or "a little more than average" (36% vs 18% in the control group; $P<.001$).

What is a POEM?

Each month, the POEMs (Patient-Oriented Evidence that Matters) editorial team reviews 105 research journals in many specialties, and selects and evaluates studies that investigate important primary care problems, measure meaningful outcomes, and have the potential to change the way medicine is practiced. Each POEM offers a Bottom Line observation and summarizes the study's objective, patient population, study design and validity, and results. InfoPOEMs, Info-Retriever and POEMS for Primary Care are registered trademarks of InfoPOEM, Inc. POEMS and Patient-Oriented Evidence that Matters are trademarks of InfoPOEM, Inc. These POEMs are copyrighted by, and published with the express permission of InfoPOEM, Inc. and may not be copied or otherwise reproduced without the prior written consent of InfoPOEM, Inc.

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High-dose zafirlukast in emergency department provides small benefit in acute asthma

Silverman RA, Nowak RM, Korenblat PE, et al. Zafirlukast treatment for acute asthma. Chest 2004; 126:1480–1489.

Clinical Question

Does high-dose zafirlukast reduce the need for hospital admission in patients with an acute asthma exacerbation, and does 1 month of zafirlukast prevent relapse?

Bottom Line

A high dose of zafirlukast (Accolate) slightly reduces the number of patients who have an extended stay in the emergency department (number needed to treat [NNT]=20). Continuing zafirlukast at a dose of 20 mg twice a day slightly improves outpatient outcomes, as well (NNT=20 to prevent relapse).

Other studies have shown that inhaled corticosteroids are better long-term monotherapy for patients with asthma than leukotriene inhibitors. It is difficult to say whether this approach should be widely adopted—although the results are intriguing, I'd like to see at least one confirmatory study. This approach is, however, simple and relatively inexpensive. (LOE=**1b**)

Study Design

Randomized controlled trial (double-blinded)

Allocation

Concealed

Setting

Emergency department (ED)

Synopsis

Zafirlukast is a leukotriene inhibitor, and the authors of this study speculate that its anti-inflammatory effect may improve outcomes in adolescents and adults with an acute exacerbation of asthma. Patients aged 12 to 65 years presenting with acute asthma were considered for inclusion if they had an forced expiratory volume at 1 second (FEV_1) of less than 70% of predicted at admission to the ED and 25 minutes after a single dose of inhaled albuterol. They were excluded if they smoked; were pregnant; had recently used steroids or leukotriene inhibitors; needed intubation; or had pneumonia, fever, or any serious comorbidity.

Patients (n=641) were randomized (allocation apparently concealed) to zafirlukast 160 mg in a single dose, zafirlukast 20 mg in a single dose, or placebo in a 1:1:2 ratio. All patients received 60 mg oral prednisone and additional doses of nebulized albuterol at 60, 120, and 180 minutes. After 3.5 hours in the ED, patients were re-evaluated, and it was determined whether they were ready for discharge or required additional care. Although physicians were encouraged to use standard criteria for this decision, the final decision was theirs alone.

Patients discharged from the ED after 4 hours entered a second phase of the study. Those who received any dose of zafirlukast continued to receive 20 mg twice per day (n=276), while patients who received placebo in the ED received matching placebo twice per day (n=270). All patients received 7 days of prednisone 20 mg twice a day, were given an albuterol inhaler, and told to resume any previous asthma medications other than leukotriene inhibitors.

The primary outcomes were the likelihood of relapse in the outpatient setting, defined as any unscheduled visit to the outpatient clinic or ED during the subsequent month, and the rate of requiring care beyond 4 hours in the ED for the initial visit (extended care). Patients kept a symptom diary during the month of outpatient follow-up, which was completed by 86% in the zafirlukast group and 81% in the placebo group. Groups were balanced at the start of the study, and analysis was by intention to treat.

Patients receiving 160 mg of zafirlukast (drug cost, approximately $10) were slightly less likely to require extended care in the ED than those receiving 20 mg or placebo (9.9%, 16.5%, and 15.0%, respectively; P=.05; number needed to treat [NNT]=20). Because we are not told how many patients actually required hospitalization, I suspect that there was no difference. During the outpatient follow-up period, patients who continued to receive zafirlukast were slightly less likely to relapse (23.6% vs 28.9%; P=.05; NNT=20). Regarding secondary outcomes, patients receiving

the high-dose zafirlukast had a lower dyspnea score after 3.5 hours in the ED than those receiving either low-dose zafirlukast or placebo, and those taking zafirlukast during the outpatient follow-up period had small advantages over those taking placebo in the symptom diary scores, although these were of questionable clinical significance.

Popular diets equally effective for losing weight

Dansinger ML. Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction. A randomized trial. JAMA 2005; 293:43–53.

Clinical Question

Which of 4 popular diets (Atkins, Zone, Weight Watchers, and Ornish) is most effective for losing weight and reducing cardiac risk factors?

Bottom Line

All 4 diets are equally effective for helping adults lose weight and reduce cardiac risk factors. Since success in this study directly correlated with adherence to the diet, it makes sense to help patients choose the diet that is easiest for them to follow, and not preferentially encourage one diet over any other. (LOE=**1b–**)

Study Design

Randomized controlled trial (single-blinded)

Allocation

Concealed

Setting

Outpatient (specialty)

Synopsis

Every week it seems as if somebody publishes another diet book that claims to be the best method for losing weight and keeping it off. In fact, very little data addresses the health effects of popular diets and even less data directly compares different diets.

The investigators enrolled 160 overweight or obese adults (mean body mass index=35; range=27–42), aged 22 to 72 years, with known hypertension, dyslipidemia, or fasting hyperglycemia. Subjects were randomized (concealed allocation assignment) to either Atkins (carbohydrate restriction), Zone (macronutrient balance), Weight Watchers (calorie restriction), or Ornish (fat restriction) diet groups. Individuals assessing outcomes were blinded to treatment group assignment.

The study attrition rate as a result of patient dropouts was high: the number of participants who did not complete the study at months 2, 6, and 12 were 34 (21%), 61 (38%), and 67 (42%), respectively. The most common reason cited by subjects for withdrawing was that the assigned diet was too hard to follow or was not resulting in enough weight loss.

Although the results were not statistically significant (P=.08), more subjects discontinued the Atkins (48%) and Ornish diets (50%) than the less extreme Zone (35%) and Weight Watchers (35%) diets. Using intention-to-treat analysis, all 4 diets resulted in similar weight loss at 1 year, with no statistically significant difference between the diets. In each of the diet groups, approximately 25% and 10% of subjects sustained a weight loss of more than 5% and 10% of initial body weight, respectively, at 1 year.

Cardiac risk factor improvement was directly proportional to the amount of weight loss and was similar among the diet groups. Self-reported dietary adherence directly correlated with the amount of weight loss and reduction in cardiac risk factors. The study was powered to have an 80% chance of detecting a weight change of 2% from baseline or a 3% difference between diets.

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Aspirin plus PPI safer than clopidogrel if there is history of GI bleeding

Chan FK, Ching JY, Hung LC, et al. Clopidogrel versus aspirin and esomeprazole to prevent recurrent ulcer bleeding. N Engl J Med 2005; 352:238–244.

Clinical Question

What is the best antithrombotic for patients with a history of upper gastrointestinal bleeding?

Bottom Line

For patients with a history of bleeding peptic ulcer, the combination of aspirin and a proton pump inhibitor (PPI) twice a day was safer than clopidogrel in terms of bleeding side effects. Although esomeprazole (Nexium) was used in this study, generic omeprazole 20 mg give twice a day provides nearly the same degree of acid suppression at a much lower cost. This study calls into question the overall safety of clopidogrel (Plavix), which has been claimed to not significantly increase the risk of bleeding. (LOE=**1b**)

Study Design

Randomized controlled trial (double-blinded)

Allocation

Concealed

Setting

Inpatient (any location) with outpatient follow-up

Synopsis

Clopidogrel has been recommended by the American College of Cardiology as the preferred drug for patients who require an antithrombotic agent to prevent heart disease but who also have a history of bleeding peptic ulcer. This study compared clopidogrel with the combination of aspirin and esomeprazole in this setting. Patients with a source of upper gastrointestinal bleeding (52% gastric ulcer, 34% duodenal ulcer, 8% both, 6% other erosions) who had healing confirmed by endoscopy were randomized to clopidogrel 75 mg daily plus esomeprazole placebo twice daily or aspirin 80 mg daily plus esomeprazole 20 mg twice daily. Groups were fairly well balanced at

the outset, allocation was concealed, and analysis was by intention to treat.

Patients were treated for 12 months. The primary outcome (hematemesis, melena, or a decrease in hemoglobin of at least 2 g/dL accompanied by endoscopic evidence of ulcer or erosion) was seen in 8.6% of the clopidogrel group and 0.7% of the aspirin plus esomeprazole group (*P*=.001; number needed to treat=13).

Three patients in the clopidogrel group had severe bleeding complications not related to the gastrointestinal tract, including 2 intraventricular hemorrhages, 1 of which was fatal; there were no bleeding complications in the aspirin group. There were more deaths in the clopidogrel group (8 vs 4), but this difference was not statistically significant. There was no difference between groups in the likelihood of adverse cardiovascular events (9 vs 11).

Clinical decision rules accurately predict stroke risk in atrial fibrillation

Gage BF, van Walraven C, Pearce L, et al. Selecting patients with atrial fibrillation for anticoagulation: Stroke risk stratification in patients taking aspirin. Circulation 2004; 110:2287–2292.

Clinical Question

Which patients with atrial fibrillation would benefit from anticoagulation?

Bottom Line

Clinical decision rules, especially the well-validated Stroke Prevention in Atrial Fibrillation (SPAF) score, can help identify which groups of patients with atrial fibrillation are likely and unlikely to benefit from anticoagulation. (LOE=**1a**)

Study Design

Decision rule (validation)

Setting

Various (meta-analysis)

Synopsis

A knee-jerk response of atrial fibrillation = anticoagulation no longer works. If the risk of stroke is low (<2%), the harms of anticoagulation generally outweigh the benefits. If the risk of stroke is high (>4%), the benefits of anticoagulation outweigh the risks for most patients. If the patient's stroke risk is in between both extremes, we have to look carefully at his or her risk for hemorrhage.

This article tested the ability of 5 clinical decision rules to accurately identify low-risk patients who don't need anticoagulation and high-risk patients who do. The validation population consisted of pooled data from 2580 patients in the aspirin arm (75 to 325 mg daily) of 6 randomized controlled trials. The mean age was 72 years, 37% were women, 46% were hypertensive, and 22% had a prior stroke or transient ischemic attack. All 5 rules were able to divide patients into low-, moderate-, and high-risk groups. However, the number of patients in the low-risk group varied from 175 to 983, and varied in the high-risk group from 223 to 1543.

Clearly, identifying a greater percentage of patients in the low- and high-risk groups is better than having too many in the intermediate group where no definitive advice can be made. A rule that did this well was the Stroke Prevention in Atrial Fibrillation (SPAF) rule. Patients who had any of the following were considered high risk by the SPAF rule: systolic blood pressure greater than 160 mm Hg, prior ischemia, recent heart failure, or left ventricular ejection fraction less than or equal to 25%. Women older than 75 years also fell into the high-risk category.

Patients who were high risk had a 3.6% risk of stroke (95% confidence interval [CI], 2.7–4.7; n=884). Patients who had none of the high-risk factors but carried a diagnosis of hypertension were considered moderate risk and had a 2.7% risk of stroke (95% CI, 1.8–4.0; n=462). Finally, low-risk patients (anyone who was not moderate- or high-risk) had a 1.1% risk of stroke (95% CI, 0.7–1.8; n=668). The authors like the CHADS2 rule, named for the elements in the score (Congestive heart failure, Hypertension, Age, Diabetes, and prior Stroke or transient ischemic attack). However, this score placed the majority of patients in the intermediate group, which is less helpful for clinical decision making.