

Raloxifene and tamoxifen both reduce breast cancer risk

Clinical question What are the relative effects of raloxifene and tamoxifen on the risk of invasive breast cancer?

Bottom line Tamoxifen (Nolvadex, Tamofen) and raloxifene (Evista) are similarly effective for reducing the risk of invasive breast cancer in postmenopausal women. Although women taking tamoxifen are at increased risk for thromboembolic events and cataracts, they report improved sexual function compared with women taking raloxifene. All-cause mortality and overall quality of life were similar in both treatment groups. (Level of evidence = 1b-)

Vogel VG, Costantino JP, Wickerham DL, et al, for the National Surgical Adjuvant Breast and Bowel Project (NSABP). Effect of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP study of tamoxifen and raloxifene (STAR) P-2 trial. *JAMA*. 2006;295:2727-2741.

Synopsis These investigators identified postmenopausal women, 35 years or older, with at least a 5-year predicted breast cancer risk of 1.66% on the Gail model. A total of 19,747 women (mean age, 58.5 years) met inclusion criteria. Study participants randomly received (concealed allocation assignment) tamoxifen (20 mg/d) or raloxifene (60 mg/d) for a maximum of 5 years. More than 94% of the women were followed for a mean of 3.9 years. The authors do not state whether individuals assessing outcomes remained blinded to treatment group assignment. Using intention-to-treat analysis, there were no significant differences between the two groups in the risk of either invasive or noninvasive breast cancer, uterine cancer, other invasive cancers, ischemic heart disease events, stroke, osteoporotic fractures, or all-cause mortality. Thromboembolic events and cataracts occurred significantly less often in the raloxifene group. A related study in the same issue (*JAMA*. 2006;295:2742-2751) reported no significant differences between the treatment groups in physical health, mental health, or depression, but the tamoxifen group reported better sexual function.

Optimal algorithm for evaluating suspected DVT is identified

Clinical question What is the best management strategy for patients with suspected deep vein thrombosis (DVT)?

Bottom line The most cost-effective algorithm for managing patients with suspected DVT was identified, although several others are nearly as good. The best approach uses a combination of a validated clinical decision rule, D-dimer test, and venous ultrasound. (Level of evidence = 1b)

Goodacre S, Stevenson M, Walloo A, et al. How should we diagnose suspected deep-vein thrombosis? *QJM*. 2006;99:377-388.

Synopsis These authors systematically reviewed the literature and identified 18 different strategies for managing patients with suspected DVT. They then evaluated a hypothetical group of 1,000 patients using each algorithm, applying reasonable estimates of test accuracy, treatment effectiveness, and the cost of testing and treatment, including the cost of applying a clinical decision rule, such as the Wells rule. They estimated a mean survival of 11.6 quality-adjusted life-years after diagnosis of DVT at age 60. The estimates were reasonable, and most of the algorithms used some combination of the Wells rule, D-dimer, and venous ultrasound. The percentage of patients with proximal DVT who would be treated appropriately with use of the algorithms ranged from 90.1% to 99.5%, and the patients without DVT who would be treated inappropriately ranged from 0.6% to 6.0%. The optimal algorithm used a latex D-dimer test as the initial screen. If patients were D-dimer negative and had a low or intermediate Wells score, DVT was considered to be ruled out. If they were D-dimer negative but at high risk based on the Wells score, an above-knee venous ultrasound was ordered. If the ultrasound was positive, they were treated; if negative, a repeat ultrasound was ordered. Patients who were D-dimer positive underwent ultrasound. If the test was positive,

they were treated; if negative, they had a repeat ultrasound. Several other algorithms were similarly cost-effective.

Preventive effects of probiotics vary by type of diarrhea

Clinical question Do probiotics prevent acute diarrhea?

Bottom line Probiotics reduce the risk of antibiotic-associated diarrhea and other types of acute diarrhea, but not the risk of traveler's diarrhea, in both children and adults. The protective effect does not vary among different probiotic strains or by mode of delivery. (Level of evidence = 1a)

Sazawal S, Hiremath G, Dhingra U, et al. Efficacy of probiotics in prevention of acute diarrhea: a meta-analysis of masked, randomized, placebo-controlled trials. *Lancet Infect Dis*. 2006;6:374-382.

Synopsis Probiotics are effective in the treatment of acute infectious diarrhea in adults and children. However, the role of probiotics in preventing acute diarrhea is less certain. These investigators thoroughly searched multiple databases—including MEDLINE, the Cochrane Registry, and references of published review articles—and personally contacted researchers known to be working in the field. Only randomized, double-blind, placebo-controlled trials in either English or French were included. Three individuals separately evaluated articles for eligibility and quality; disagreements were resolved by consensus discussion. A total of 34 trials including 4,844 patients aged 6 months to 71 years met the inclusion criteria. Overall, probiotics reduced the risk of acquiring diarrhea by 33% (95% confidence interval, 22%-44%; number needed to treat = 15, CI 11-22). In subgroup analyses, probiotics significantly reduced the risk of antibiotic-associated diarrhea and acute diarrhea of other types but not traveler's diarrhea. Probiotics were more effective in children, and the protective effect did not vary significantly among different strains or by mode of delivery (ie, capsules, tablets, granules, or powder).

Metformin helps children and adolescents lose weight

Clinical question Does metformin lead to weight loss for obese children and adolescents?

Bottom line For obese 9- to 18-year-olds, metformin (1 g twice daily) resulted in a mean weight loss of approximately 10 pounds at the end of 6 months of treatment. Larger and longer studies are needed to support the effectiveness and safety of this regimen. (Level of evidence = 1b-)

Srinivasan S, Ambler GR, Baur LA, et al. Randomized, controlled trial of metformin for obesity and insulin resistance in children and adolescents: improvement in body composition and fasting insulin. *J Clin Endocrinol Metab*. 2006;91:2074-2080.

Synopsis Participants were obese 9- to 18-year-olds (13 boys, 15 girls) who were treated in an endocrine clinic. All had clinical evidence of insulin resistance but did not meet the criteria for diabetes. Patients were randomized (double-blinded) to metformin, 1g twice daily, or placebo for 6 months. This was followed by a 6-month crossover to the other treatment, with a 2-week wash-out period in between. There were equal numbers of children at Tanner stages 1 and 2 and at Tanner stages 3 to 5 at the start of the study. Mean body mass index (BMI) was 35 kg/m². Standardized information on exercise and healthy eating was given to all patients. Four patients dropped out during the study, none because of medication side effects. At the end of the active treatment period, significant benefits were observed for weight, BMI, abdominal circumference, and fasting insulin levels. The mean sizes of treatment effects at the end of the 6-month period of active therapy compared with placebo were weight loss of 4.35 kg, BMI decrease of 1.3 kg/m², waist circumference decrease of 2.8 cm, and fasting insulin decrease of 2 mU/L. Data were not presented to calculate a number needed to treat.

Levels of evidence are explained at <http://www.infopoems.com/levels.html>.

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