fewer puffs (1 puff of 220 µg) than Vanceril DS (4 puffs of 84 µg) to accomplish more. Flovent costs approximately $1.70 per day, while an equivalent dose of beclomethasone costs $4.15 per day. Fewer puffs will likely lead to greater compliance. Cheaper, more effective, and easier to use — fluticasone is the better inhaled steroid for persistent asthma.

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Does Raloxifene Reduce Breast Cancer Risk?

Cummings SR, Eckert S, Krueger KA, et al. The effect of raloxifene on risk of breast cancer in postmenopausal women. JAMA 1999; 281:2189-97.

Clinical question **Do women taking raloxifene have a lower risk of invasive breast cancer?**

Background Raloxifene, a selective estrogen receptor modulator, offers the possibility of selectively inhibiting estrogenic effects in the breast and endometrium while stimulating bone mineralization. This clinical trial assesses the impact of raloxifene on women given a new diagnosis of breast cancer.

Population studied A total of 7705 postmenopausal women were enrolled from 180 centers in the United States and Europe. The women included in the study were at least 2 years postmenopausal (average age = 66 years) and were overweight (body mass index > 25). Most of the patients were white (96%). All of these women had osteoporosis, defined as bone density more than 2.5 standard deviations below the mean for normal young women or the presence of vertebral fractures.

The women received a baseline breast examination and mammography; those with definite or suspected breast cancer or a history of breast cancer, abnormal uterine bleeding, or thromboembolic disease were excluded. Twelve percent had a family history of breast cancer, and the breast cancer incidence in the placebo group was approximately 2% in 5 years. Thus, the study population was at relatively low risk for breast cancer. Information on other risk factors for breast cancer and a broader ethnic base would have helped family physicians assess the generalizability of the results to their practices.

Study design and validity This was a double-blind placebo-controlled trial with 3 arms. Patients received either placebo, or raloxifene at a dose of 60 or 120 mg daily. All participants received 500 mg of calcium and 400 to 600 international units of vitamin D daily. The subjects were examined every 6 months for 3 years, with mammograms done at years 2 and 3; a subsample received endometrial ultrasound and biopsies. Of the women in the placebo group and the raloxifene groups, 75% and 78%, respectively, finished the trial. The raloxifene groups were pooled for comparison with placebo; analysis was by intention to treat. Results were also analyzed after stratification for estrogen receptor status.

In general, the methodology of this study was good. The placebo and raloxifene groups were similar at the beginning of the study. The low risk of breast cancer and the relatively short follow-up strengthen the results. Significant weaknesses include the loss of 25% of the subjects to follow-up and the lack of control for confounding variables, such as other risk factors that might influence the incidence of breast cancer.

Outcomes measured The primary outcome was incidence of breast cancer. Secondary outcomes included rates of endometrial cancer and thromboembolic disease, and incidence of symptoms. Other outcomes important to the hormone replacement therapy decision, including symptomatic fractures, patient satisfaction, cost, and quality of life were not addressed.

Results Subjects receiving raloxifene were significantly less likely to receive a diagnosis of breast cancer during the 5 years of the study (relative risk [RR] = 0.24; 95% confidence interval [CI], 0.13 - 0.44). One hundred twenty-six women would need to be treated with raloxifene for 3 years to avoid one diagnosis of breast cancer. This decrease occurred with estrogen-receptor–positive cancers (RR = 0.10; 95% CI, 0.04 - 0.24).

Subjects taking raloxifene had no increase in endometrial cancer but a higher rate of thromboembolic disease (RR = 3.1; 95% CI, 1.5 - 6.2); the number needed to harm (NNH) was 143 for thromboembolic disease and 500 for pulmonary embolism. Hot flashes and leg cramps were significantly more frequent in women taking raloxifene (NNH = approximately 25 and 33, respectively), and rates of vaginal bleeding and breast pain were similar to that of the controls. There were no differences in mortality.

Recommendations for clinical practice **This study provides good evidence that in postmenopausal women raloxifene delays or prevents breast cancer without increasing the risk of endometrial cancer. We do not know whether women live longer as a result of this therapy.**

The relatively low risk of the population in this study strengthens the conclusion that raloxifene prevented breast cancer even in women at low risk (2%). The increased risk of thromboembolic disease is real, though minimal, and should be dis-

cussed with patients. These findings are consistent with a recent systematic review.[1]

This study does not address the applicability to women in perimenopause; the acceptability of raloxifene to women over a long period of time, particularly those with worse symptoms of estrogen deficiency; and the prevention of clinically important fractures and cardiovascular morbidity. Clinicians should not recommend raloxifene routinely until good quality information about these issues becomes available.[1]

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Medical Therapy for Stable Angina

Heidenrich PA, McDonald KM, Hastie T, et al. Meta-analysis of trials comparing β-blockers, calcium antagonists, and nitrates for stable angina. JAMA 1999; 281:1927-36.

Clinical question **Should we use β-blockers (BBs), calcium channel blockers (CCBs), or long-acting nitrates (LANs) as first-line therapy for patients with stable angina?**

Background The choice of preferred agent for stable angina remains controversial. BBs have been shown to reduce mortality following myocardial infarction and are recommended by some experts. However, others believe CCBs are equally efficacious and are better tolerated than BBs. Others recommend LANs. No agent has been proved superior for treating stable angina. The authors performed a meta-analysis to assess the relative efficacy and tolerability of these agents.

Population studied All patients in studies in this meta-analysis had stable angina. Many studies comparing BBs with CCBs excluded patients with recent myocardial infarction, heart failure, bradyarrhythmias and heart block, diabetes mellitus, and chronic obstructive pulmonary disease.

Study design and validity This meta-analysis was methodologically sound. The authors searched MEDLINE (1966-1997) and EMBASE (1974-1997) using explicit criteria and reviewed bibliographies from identified trials. Studies were eligible for inclusion if they were randomized controlled trials or crossover trials comparing agents from different classes and were written in English. The authors did not attempt to locate unpublished articles; however, publication bias against negative results is unlikely, since 75% of the studies showed no difference between agents. The authors reviewed the abstracts of 48% of the non-English articles: No data were found that contradicted this study's findings.

Data extraction was performed independently. Statistical analyses were appropriate. The lack of a systematic review of quality of the included studies is a minor concern with this study.

Outcomes measured The effectiveness of the different therapies was evaluated by measuring the number of angina episodes per week, the number of nitroglycerin tablets taken per week, total exercise time, and time to 1-mm ST segment depression during exercise. Tolerability was assessed using the combined rate of subject withdrawal because of adverse events, defined as death or cardiac or noncardiac symptoms. All-cause mortality was not assessed; most trials were too small or too short to address this important outcome.

Results Of the 90 studies included in the analysis, 72 compared BBs with CCBs. The mean duration of these studies was 8 weeks; only 2 were longer than 6 months. There were no significant differences reported between BBs and CCBs for cardiac death or myocardial infarction, nitroglycerin use per week, or time to 1-mm ST segment depression with exercise. Patients taking CCBs had slightly longer exercise times (effect size = 0.1; P = .05). Patients taking BBs had 0.31 fewer episodes of angina per week (P = .05) and were less likely to withdraw because of adverse effects (odds ratio = 0.72; 95% confidence interval, 0.6 - 0.86). The absolute difference in withdrawal rates was 2; that is, for every 100 patients treated with BBs, 2 fewer patients suffered an adverse event leading to study withdrawal than with patients taking CCBs.

Subgroup comparisons showed fewer episodes of angina among patients taking BBs than with patients taking nifedipine or short-acting CCBs. The odds of withdrawal because of adverse events were lower for BBs than with nifedipine, short-acting CCBs, and long-acting CCBs. In comparison with BBs, nifedipine was the most poorly tolerated CCB.

There were no differences noted between agents in the 12 studies comparing LANs with CCBs. In the 6 studies comparing BBs with LANs, there was a trend toward increased nitroglycerin use among patients taking LANs (2 tablets per week, P = .08), though there were significant differences in the 3 trials evaluating this outcome.

Recommendations for clinical practice **BBs are better tolerated than CCBs and are associated with fewer episodes of angina per week. They**