of β_2-agonist use. These effects may not pertain to other high-dose inhaled steroids, as the authors cite an abstract that showed no benefit in pulmonary function from flunisolide in a similar study. Using the current average wholesale price for the budesonide Turbuhaler, the cost to prevent one office or ED visit would be approximately $1000. This would imply a fairly high cost-to-benefit ratio; formal cost-benefit analysis is yet to be done.

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Which Inhaled Corticosteroid for Asthma?

Raphael GD, Lanier RQ, Baker J, Edwards L, Rickard K, Lincourt WR. A comparison of multiple doses of fluticasone propionate and beclomethasone dipropionate in subjects with persistent asthma. J Allergy Clin Immunol 1999; 103:796-803.

Clinical question **Which inhaled steroid — fluticasone (Flovent) or beclomethasone (Beclovent, Vanceril) — is more effective for treating persistent asthma?**

Background The National Institutes of Health's treatment guidelines for persistent asthma recommend the use of inhaled corticosteroids. Although the guidelines recognize categories of inhaled steroids and provide guidance for the use of low, medium, and high dosages, none is recommended.

Population studied A total of 399 nonsmoking men and women aged 12 years and older with chronic asthma requiring daily inhaled steroids for at least 6 months were enrolled. Each person had taken 8 to 12 puffs per day of either beclomethasone or triamcinalone for at least 1 month before enrollment. Screening and baseline forced expiratory volume in 1 second (FEV_1) values were between 45% and 80% of predicted normal. Subjects had reversible lung function (≥12% increase in FEV_1 after 2 puffs of albuterol). Continuation of theophylline or salmeterol was allowed if taken at stable and approved doses and if the morning dose was withheld before all study visits. The only other permitted asthma medication was the albuterol metered-dose inhaler (Ventolin) for symptomatic relief. Exclusion criteria included the use of oral or intravenous steroids, leukotriene modifiers, or nedocromil sodium for 1 month before the study.

Study design and validity This randomized double-blind double-dummy parallel-group clinical trial was conducted at 23 specialty asthma and primary care study centers and occurred over 12 weeks. There were 4 treatment groups: low-dose fluticasone (44 µg/puff, 2 puffs twice daily); medium-dose fluticasone (110 µg/puff, 2 puffs twice daily); low-dose beclomethasone (42 µg/puff, 4 puffs twice daily); and medium-dose beclomethasone (42 µg/puff, 8 puffs twice daily).

Before the 12-week randomization, there was a 2-week single-blind run-in period. During this phase, subjects took beclomethasone (42 µg/puff, 4 puffs twice daily) with a placebo instead of their usual inhaled steroid. Eligibility for the study was evaluated, compliance with medication use was assessed, and a baseline was established.

Spirometry was done at screening (before the run-in period), at baseline (after the run-in period), and after 1, 2, 4, 6, 8, 10, and 12 weeks. Subjects kept diary cards documenting supplemental albuterol use, morning and evening peak expiratory flow rates (PEFRs), night awakenings caused by asthma, and asthma symptoms on a scale of 0 to 3 (where 0 = none and 3 = severe).

This well-designed study with 4 demographically similar treatment groups took great care to ensure compliance and similar knowable patient baselines using the run-in phase. Spacers were not used and 8 puffs twice daily of 42 µg/puff beclomethasone was used instead of 4 puffs twice daily of the 84 µg/puff product.

Outcomes measured Outcomes measured included FEV_1, daily albuterol use, asthma symptoms, PEFRs, and nighttime awakenings due to asthma.

Results Fluticasone at both the low and medium dose improved FEV_1 by 0.31 L (14%) and 0.36 L (15%), respectively, compared with improvements of 0.18 L (8%) and 0.21 L (9%) with the low and medium doses of beclomethasone. In each outcome category, with the exception of night awakenings, fluticasone bested beclomethasone: morning PEFR (P <.001), evening PEFR (P = .06), puffs per day of albuterol (P = .004), percent days without albuterol use (P = .01), asthma symptom scores on a 0 to 3 scale (P = .024), and percent days without symptoms (P = .027). Overall, greater improvements in pulmonary function parameters occurred with fluticasone treatment (P <.034). Similar side effect and withdrawal rates were reported between the various groups.

Recommendations for clinical practice **When treating persistent asthma, fluticasone is more effective than beclomethasone in equivalent doses. This is true for both disease-oriented outcomes (eg, spirometry) and for patient-oriented outcomes (eg, fewer asthma attacks). Fewer attacks means less rescue albuterol, which translates into lower patient expense. Flovent requires**

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-