In patients with chronic obstructive pulmonary disease (COPD), do inhaled corticosteroids (ICSs) reduce the progression of airflow limitation?

**Methods**

**Data sources:** Medline (1966 to February 2003), CINAHL (1982 to February 2003), International Pharmaceutical Abstracts (1970 to February 2003), and the Cochrane Controlled Trials Register, references of retrieved articles, and experts in the field.

**Study selection and assessment:** full reports of randomised controlled trials of ICSs in patients with COPD, had >1 year of follow up, examined change in FEV₁ over time, patients with asthma were excluded, and patients were studied when COPD was stable.

**Outcomes:** progression of airflow limitation measured by annual rate of change in FEV₁.

### Main Results

8 trials (n = 3715) were included. All trials were >2 years in duration (range 24–40 mo). The ICSs studied were fluticasone, triamcinolone, budesonide, and beclomethasone. ICSs reduced the rate of decline in FEV₁ more than did placebo (table). Meta-analysis of trials of high dose ICS regimens (4 trials, 2416 patients) also favoured ICSs (table).

### Conclusion

In patients with chronic obstructive pulmonary disease, inhaled corticosteroids reduce the progression of airflow limitation.

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**Commentary**

COPD is largely a disease of vulnerable smokers in whom the normal age related decline in lung function is accelerated from a mean of 30 ml/y to 60 ml/y. Unlike asthma, the airflow obstruction and airway inflammation of COPD respond poorly to corticosteroids. The review of randomised controlled trials by Sutherland et al shows a statistically significant reduction in the annual rate of decline in FEV₁ of 7.7 ml/y with higher dose regimens, and patients with more severe disease obtained greater benefit. Although the absolute reduction was small, it represents a reduction in the rate of decline of about 15% in smokers compared with a reduction of about 50% as a result of smoking cessation.1

COPD is now our fourth most common cause of death, and no drugs apart from oxygen alter the natural history of the disease. But should any intervention that slows the inexorable decline in lung function be welcomed? Arguably, the small advantage in terms of reduced decline in FEV₁ is of little clinical relevance. Furthermore, widespread introduction of high dose ICSs for all patients with COPD would be expensive given the prevalence of the disease and its long term course. In my opinion, we should put the resources into vigorous smoking prevention and cessation programmes that are more effective in terms of preserving lung function (as well as preventing cancer and heart disease). Pressure to prescribe these drugs for many patients with essentially irreversible airflow obstruction can be resisted but emphasises the importance of distinguishing asthma from COPD.

The discrepancy between the results of the systematic reviews of Highland et al2 and Sutherland et al will also fuel current anxieties about the validity of meta-analysis, especially as nearly identical trial data were incorporated in these 2 reviews. In fact, the rate of decline in FEV₁ in both analyses was very similar (5 ml/y and 7.7 ml/y, respectively) but the former failed to reach statistical significance. The differences emphasise how apparently uncontroversial assumptions made during data extraction can have substantial effects on the primary outcome and might lead to very different recommendations in “evidence-based” clinical guidelines. Readers of meta-analyses need to be vigilant as to the absolute size of the effects of any intervention and aware that pooling trial data can be a hazardous activity.

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**Inhaled corticosteroids vs placebo for chronic obstructive pulmonary disease at 24–40 months**

<table>
<thead>
<tr>
<th>Trials</th>
<th>Annual reduction in FEV₁ decline (95% CI)</th>
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<tbody>
<tr>
<td>All trials (8 trials, n = 3715)</td>
<td>7.7 ml/y (1.3 to 14.2)</td>
</tr>
<tr>
<td>Trials with high-dose regimens (4 trials, n = 2416)</td>
<td>9.9 ml/y (2.3 to 17.5)</td>
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*Values are means. CI defined in glossary. A random effects model was used.