

dysfunction. Perhaps the dyspnoea was due to obesity or poor cardiovascular conditioning, which obviously does not respond to bronchodilator therapy. Similarly, the anxiety, depression, pain, and general discomfort reported by many of the study participants, which the authors consider as evidence "that mild COPD does cause impairment," is highly unlikely to respond to any bronchodilator.

I strongly disagree with the authors' speculation that "short-term improvements in lung function may help patients to retain higher levels of activity for longer." This seems like disease mongering (selling sickness) to me, as well as inappropriate author optimism; two of the authors were employees of the drug company which makes tiotropium, with sales of 3 billion Euros in 2007 [Boehringer financial report, 2008]. The recently concluded UPLIFT study showed absolutely no difference in the decline in lung function for COPD patients randomised to tiotropium for four years when compared to those taking a placebo inhaler every morning.⁷

Considering the high cost of tiotropium, its potential for malignant arrhythmias and cardiovascular death in current or former smokers,⁸⁻¹⁰ and lack of efficacy in current or former smokers with normal spirometry or mild airway obstruction, a major professional society of internal medicine specialists has stated that inhalers for COPD should not be considered unless FEV₁ has been documented to be below 60% predicted.³ I strongly disagree with the statement that "it is imperative that COPD patients receive appropriate treatment, including preventative interventions, as early as possible".¹¹⁻¹³

More than half of the participants remained current smokers during the Johansson study. Is it ethical for investigators to withhold the only treatment proven to halt the rapid loss of lung function in smokers with COPD? Instead of a quick and easy prescription for a COPD inhaler, all available resources should be used by GPs to help smokers to quit smoking, including treatment with bupropion or varenicline.¹⁴ I worry that many smokers who are prescribed an inhaler for COPD feel that they don't need to try to stop smoking. A survey is needed to confirm my suspicion.

In summary, a prescription for tiotropium in smokers with an FEV₁ above 60% predicted is likely to cause more harm than good.

Conflict of interest declaration

During the past three years, the author has received payments for consulting on spirometry quality assurance programs for phase III clinical trials from Pfizer (varenicline for smoking cessation in patients with COPD) and InterMune (for patients with idiopathic pulmonary fibrosis). He has received no consulting or travel expense reimbursement from any companies which make pulmonary function equipment or spirometers.

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Authors' reply

We thank P. Enright for his comments to our clinical trial¹ which studied the effect of tiotropium treatment in patients with mild disease according to the COPD guidelines of the Swedish Society of Respiratory Medicine from 2003.² While the Swedish guidelines classify patients with a post-bronchodilator (pBD) FEV₁ >60% as "lindrig" COPD (= mild), the Global Initiative on Obstructive Lung Disease⁵ considers COPD patients with a pBD FEV₁ >80% and symptoms as having mild disease, and those with a pBD FEV₁ below 80% as at least moderately affected.

We do not concur with Enright's assumption that "it is highly unlikely that any respiratory symptoms such as dyspnoea reported by smokers with an FEV₁ above 60% predicted are due to impairment of lung function". In a recent study, Ofir et al.³ demonstrated dynamic hyperinflation, increased exercise-induced dyspnoea and decreased max. oxygen consumption and power output (approx. 20%) in 21 COPD patients with an average pBD FEV₁ of 91% predicted. Limitations during exercise are associated with extensive small airways dysfunction in these patients whose lung function at rest appears to be relatively preserved. Consequently, these patients are likely to benefit from bronchodilation irrespective of the improvements observed with spirometry conducted under resting conditions and should receive appropriate treatment, which of course includes consideration of options to foster smoking cessation.^{4,5}

We disagree with Enright's comments on cardiovascular safety. In a recently published randomised placebo-controlled 4-year trial⁶ in 5993 patients tiotropium reduced cardiac morbidity (relative risk for cardiovascular events 0.81; 95%CI 0.68 to 0.97) and cardiac

mortality (relative risk 0.80; 95%CI 0.64 to 1.02).⁷

For the reasons above we do not agree with Enright that a prescription of tiotropium in smokers with an FEV₁ above 60% predicted is likely to cause more harm than good.

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