Exhaled nitric oxide and COPD

To the Editors:

We were interested to read the paper by LEHTIMÄKI *et al.* [1] recently published in the *European Respiratory Journal*, in which those authors reported that ''high pre-treatment levels of $J'_{aw,NO}$ [bronchial nitric oxide flux] are related to symptom relief and improvement of airway obstruction'' when inhaled fluticasone is given to patients with chronic obstructive pulmonary disease (COPD). Their data complement those which we ourselves have recently published [2].

In their cohort of patients, only five (12.5%) out of 40 demonstrated an objective improvement in airway calibre following inhaled fluticasone (change in forced expiratory volume in 1 s of $\geqslant$12% and/or $\geqslant$200 mL), a proportion that is similar to that reported in most other studies. Somewhat surprisingly, the number of patients who show symptomatic improvement with inhaled steroid was higher (50% had a change in St George's Respiratory Questionnaire of $\geqslant$4), but this may have been influenced by the fact that the study was not blinded. Overall, these changes were associated with small but statistically significant reductions in both $J'_{aw,NO}$ and the fraction of exhaled nitric oxide (F_{ENO}) at a flow rate of 50 $mL \cdot s^{-1}$.

In COPD, it is critical to know the extent to which a biomarker may be used to predict the response to treatment, particularly given that response rates to inhaled steroids are so low. In our study, using receiver operating curve analyses, we found F_{ENO} to be only a weak predictor of steroid response, with a positive predictive value of 67% at a cut-off point of 50 ppb. More importantly, the negative predictive value was high (82%), implying that F_{ENO} measurements can be used to predict when a response to treatment is unlikely [2].

It is important for LEHTIMÄKI *et al.* [1] to provide similar information from their own dataset. At present, their conclusions are open-ended and leave the reader with doubts as to whether the relationship between exhaled nitric oxide and the response to inhaled steroid in COPD has any clinical utility. The publication of additional data would help to clarify this issue.

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Statement of Interest: A statement of interest for D.R. Taylor can be found at www.erj.ersjournals.com/misc/statements.dtl

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2 Dummer JF, Epton MJ, Cowan JO, *et al.* Predicting corticosteroid response in chronic obstructive pulmonary disease using exhaled nitric oxide. *Am J Respir Crit Care Med* 2009; 180: 846–852.

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From the authors:

We would like to thank D.R. Taylor and J. Dummer for their comments on our recent paper [1]. In the paper, we reported that higher bronchial nitric oxide flux ($J'_{aw,NO}$) values were associated with more likely symptom relief during fluticasone treatment in patients with chronic obstructive pulmonary disease (COPD). We agree with D.R. Taylor and J. Dummer that positive and negative predictive values (PPV and NPV, respectively) for certain cut-off points of $J'_{aw,NO}$ would help the clinician to judge the applicability of $J'_{aw,NO}$ to predict steroid-responsiveness in COPD.

We have now reanalysed the data (using SPSS 12.0.1 software; SPSS Inc., Chicago, IL, USA) by using receivers operating characteristics. Baseline $J'_{aw,NO}$ was a significant predictor of symptom relief during fluticasone treatment (area under the curve 0.722; $p=0.018$). At a cut-off point of 0.7 $nL \cdot s^{-1}$, PPV for symptom relief was 83% and NPV was 56%, suggesting that at this cut-off point $J'_{aw,NO}$ is a moderately accurate predictor of good treatment response but not a useful measure to exclude symptom relief.

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