**Reply to “Adrenal Suppression with inhaled corticosteroids: the seed and the soil”**

Dear Editor,

We agree with the authors that multiple factors can affect an individual’s likelihood of developing adrenal suppression whilst using corticosteroids. We did assess these in our previous paper [1].

The issue of airway calibre is relevant to drug deposition and exposure. However, there are differences between the cited cohort [2], and ours. That study cohort was 11 asthmatic patients, mean age 45 years, and an FEV11 (% predicted) of 54% [2]. Our discovery cohort included 499 children, mean age 11.6 years, FEV1 (% predicted) of 88% [1]. This represents considerably better respiratory function, with a corresponding increase in lung deposition. In our COPD validation cohort, a smaller effect size was noted, and this may be related to many factors including the older ages, co-morbidities and potentially decreased exposure, as suggested by the authors. Despite this, 22% of our COPD patients showed biochemical suppression [3].

Pharmacology of the drug will also have a role. However, in contrast to the systematic review presented [4], adrenal suppression was not more prevalent with fluticasone in our study [1], but this may be because we also included oral (rescue and/or maintenance asthma therapy), and intranasal (hay fever) corticosteroids use in our analysis to obtain a figure for the overall steroid burden. This may account for the different findings.

Where we do completely agree with the authors is that the safest dose of corticosteroid is the lowest effective maintenance dose for that patient, whatever personalisation of therapy is being considered.

Yours faithfully,

Dr Dan Hawcutt, Dr Ben Francis, Prof Sir Munir Pirmohamed

References

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2. Brutsche, M.H., et al., *Comparison of pharmacokinetics and systemic effects of inhaled fluticasone propionate in patients with asthma and healthy volunteers: a randomised crossover study.* The Lancet. **356**(9229): p. 556-561.

3. Hawcutt, D.B., et al., *Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study.* The Lancet Respiratory Medicine.

4. Lipworth, B.J., *Systemic adverse effects of inhaled corticosteroid therapy: a systematic review and meta-analysis.* Archives of Internal Medicine, 1999. **159**(9): p. 941-955.