

## M.A. Puhan

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**Statement of Interest:** None declared.

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### From the authors:

We agree with M.A. Puhan's letter regarding the need for full reporting of important clinical end-points and appropriate statistical analysis in randomised controlled trials in chronic obstructive pulmonary disease, the need for which is demonstrated by our robust meta-analysis on cardiovascular outcomes [1].

First, the manufacturers of other inhaled bronchodilators should provide comprehensive listings of adverse events similar to those available for salmeterol–fluticasone. The present systematic review is limited by the paucity of data on budesonide, in a similar manner to our previous analysis on the outcome of pneumonia [2]. However, the subsequent availability of data on budesonide allowed us to conduct appropriate intention to treat meta-analysis on pneumonia, without censoring participants [3]. This analysis demonstrated no conclusive differences between inhaled fluticasone and budesonide on the risk of pneumonia.

Secondly, the concerns about the low absolute incidence of cardiovascular events in the trials are unfounded. The low

absolute incidence is unlikely to have significant impact on measures of relative treatment effect in our meta-analysis, because there were sufficient numbers of trial participants and cardiovascular events for us to ascertain reasonably precise estimates (narrow 95% confidence intervals) of the cardiovascular effects of inhaled corticosteroids.

Thirdly, any potential misclassification of outcomes is likely to be non-differential, and would not affect our point estimates, although it may result in some imprecision, because all the randomised controlled trials in our analysis were double-masked.

Finally, we strongly agree with M.A. Puhan that the practice of medicine should be evidence based. The "positive" opinions of inhaled corticosteroids proffered by academics should be critically examined for the hierarchy of evidence, whether they are based on randomised controlled trials or "expert" opinion. These should also be critically evaluated in light of the pervasive issue of publication bias towards positive results in pharmaceutical company-sponsored research of inhaled corticosteroids [4].

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### From the authors:

M.A. Puhan raises several issues that are frequently used to argue against the use of inhaled corticosteroids (ICS) in chronic obstructive pulmonary disease (COPD). First, he implicitly equates hormone replacement (HRT) and celecoxib therapies with the use of ICS in COPD. This is neither fair nor justified based on the existing literature. Unlike these drugs, ICS have