NNT from the MIASMA study was 41, so the findings were consistent.

Pointedly, neither of these studies looked at any inflammatory outcomes. Although adding a LABA may reduce exacerbations in a complementary manner to ICS, this is likely to be due to stabilising airway smooth muscle rather than potentiating the anti-inflammatory activity of the ICS. For example, in a study of inflammatory markers,[3] doubling the dose of fluticasone from 250 µg/day to 500 µg/day reduced exhaled nitric oxide and adenosine monophosphate hyperresponsiveness more effectively than adding salmeterol to the 250 µg dose. In other words, while adding salmeterol in preference to a higher dose of ICS might reduce exacerbations and exhibit putative steroid sparing activity, this will occur at the expense of worsening anti-inflammatory control. Without monitoring inflammation in patients who are asymptomatic on ICS/LABA combination inhalers, clinicians may be lulled into a false sense of security and overlook potential long term damage from untreated airway inflammation.

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Authors' reply

We appreciate the opportunity to respond to the issues raised by Barnes and Lipworth. However, with regard to calculating the number needed to treat (NTT), it is not clear that clinicians necessarily find this a useful measurement.[1] Most meta-analysis techniques use a weighted pooled outcome measurement that takes into account the different sample sizes and/or variances of each individual study measurement. The crude simple sum of events in both treatment groups that Barnes and Lipworth have suggested using does not. When the weighted technique is applied to the whole data set, under a fixed effects model this gives a pooled NNT of 58.4 (95% CI 32.6 to 278.3)—nearly double the number calculated by the crude method.

NNT refers to a specific time and this calculation does not take account of the fact that nearly half the studies ran for 12 weeks and the other half for 24 weeks (one for 26 weeks). The NNT for the 12 week studies was 75.5 (95% CI for the probability difference crosses zero) and for the 24 week studies it was 35.4 (95% CI 18.2 to 619.9). The point estimates for the two groups of studies are concordant in that 2 × 35.4 is close to 75. All but one of the studies analysed for exacerbations in the original MIASMA paper[2] ran for 24 weeks (the other study ran for 26 weeks) so that, if only the 24 week studies are used, our paper and the MIASMA paper agree.

Barnes and Lipworth also raise the issue of whether surrogate markers of airways inflammation such as exhaled nitric oxide and adenosine monophosphate responsiveness are preferable to clinical measures such as severe exacerbations, lung function, night wakenings, and rescue β agonist use. The advantage of these clinical measures is that they represent relevant validated methods to assess long term asthma control and the risk of morbidity and mortality; this is not the case with the surrogate inflammatory markers. For this reason we consider that the findings from our meta-analysis should provide clinicians with greater confidence when deciding the dose of inhaled corticosteroid at which to consider adding salmeterol at Step 3 in the asthma guidelines.

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ERRATUM

The name of the last author was missed from abstract number S40, *Thorax* 2005; **60**(suppl II):ii16. The correct listing of authors is: A Laverty[1], P Weller[2], A Jaffe[1] 1.Portex Respiratory Unit, Great Ormond Street Hospital for Children, London; 2. Centre for Measurement and Information in Medicine, City University, London.

The journal apologises for this error.