in evaluating asthma is to achieve the goals of asthma care: reduce symptoms and exacerbations. NHLBI [2] and the Cochrane Library Database [3] have used formal evidence-based criteria to review the literature and have concluded that inhaled corticosteroids are the preferred initial controller therapy for persistent asthma.

Rather than trying to re-evaluate data, new studies should be designed with alternative therapies that provide greater improvement in lung function, better symptom control and fewer exacerbations, with the understanding that the differences in response should also take into consideration the variable nature of the asthma.

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From the authors:

We thank D.A. Stempel, for the opportunity to restate and clarify the dialogue we had hoped to initiate with our paper [1]. As described in our paper, the primary efficacy results from these trials have previously been published. The message of our present paper, different from that of the letter by D.A. Stempel, is therefore not one of comparisons of drug treatments. In fact, there was no presentation or discussion of such data in our paper. Instead, we have engaged in an activity that he dismisses as an "intellectual exercise", with the hope of spurring further research and debate in the critical area of understanding asthma control.

The rationale for our work was to provide empirical evidence of the known variability of asthma as reflected by the key measures describing the disease process. In this context, we point out the inherent difficulties in studying this disease, particularly when relating it to haplotype associations. As D.A. Stempel notes, the aim of asthma treatment is control of the disease. Efforts to define and accurately validate the important clinical measures of this goal have provoked much debate, and uncertainty remains about which outcome or combination of outcomes in asthma will define and serve to measure control of this disease (just as fracture risk has been identified in osteoporosis, for instance). Unlike our appreciation of the relationship between bone mineral density and fracture risk in osteoporosis, or blood pressure and stroke risk in hypertension, we have a limited understanding of the clinical relevance of the measured surrogate markers (e.g. forced expiratory volume in one second, wheezing) in asthma.

The variable nature of asthma, which is the focus of our paper, is a confounding factor that makes the task of understanding how to control the disease all the more difficult. Our results show that commonly used clinical end-points measure different aspects of the disease state. These end-points may not capture adequate information to serve as predictors of long-term response to therapy. Our paper clearly points to the urgent need to frame the debate about asthma control in terms of clinically relevant outcomes, and the response to treatment in terms of relevant clinical markers.

D.A. Stempel's simple view of the evidence as reflected by published mean values that are summarised in meta-analyses does not begin to account for the complexity of measuring and understanding asthma control.

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