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From the authors:

We would like to thank P. Enright for giving us the opportunity to clarify some issues raised by the recently published interpretative strategies for lung function tests [1]. P. Enright's letter is important in that it reinforces our shared belief that guidelines are always relative and complete consensus is a utopian ideal. It also clarifies why he chose not to be listed among the authors of this section, and shows the difference in perception of time among individuals. Our records show that there was a Task Force meeting in Stockholm in 2002, which was almost entirely devoted to the divergent opinions about interpretation, most of them raised by P. Enright. Over the next year, we had a number of additional discussions by telephone and e-mail before a final vote was taken in Vienna in 2003.

The first point raised by P. Enright addresses the interpretation of a low forced expiratory volume in one second (FEV₁)/vital

capacity (VC) when the FEV₁ is normal. We recognise that figure 2 and table 6 do not specifically include the possibility that such a pattern may be a normal variant, but we are confident that the average reader will be careful enough to note this possibility is clearly included in the accompanying text. The text also stresses that an interpretation of airflow obstruction will depend on the prior probability of lung disease and on additional tests. We share P. Enright's concern that relying only on FEV₁/VC to establish treatment may be wrong, but we believe the possibility of disease must be considered in subjects with this pattern. In fact, although his letter claims "no associations with clinical disease or increased risk of future disease have been established for this pattern", another of his recent publications notes that this very spirometric pattern is associated with an increased risk of death [2]. It should also be noted that in particular populations, *e.g.* athletes with large lungs, this pattern may be present due to unequal growth of airways and lung parenchyma, whereas in asthmatic patients this may be due to airway narrowing. Distinguishing between these two conditions is an imperative task to help patients.

P. Enright also questions whether the characterisation of the pattern of normal FEV₁/VC with a low VC and normal total lung capacity (TLC) is consistent with airflow obstruction. This concern appears to be based mostly on the lack of studies of clinical correlates and outcomes associated with this pattern, as if studies on lung mechanics should not count much in interpreting lung function tests. A number of studies have indeed shown that a number of asthmatics exhibit a similar decrease in FEV₁ and VC or FVC after they have been exposed to inhaled agents that are known to narrow or close the airways without a change in TLC [3, 4]. This has also been reported in chronic airflow obstruction [5] and the mechanism has been reproduced in healthy subjects [6, 7]. Altogether, these data are the foundation of the document's cautious statement that a normal FEV₁/VC with low FEV₁ and normal TLC may be consistent with airflow obstruction, an interpretation offered in the 1993 European Respiratory Society (ERS) guidelines on lung function testing [8].

We agree that there is a risk for the over-treatment of chronic obstructive pulmonary disease (COPD), but we believe the major part of this risk is not in the interpretative strategies published by the American Thoracic Society (ATS)/ERS (and supported by most of the Task Force members). We believe the suggestion to use the statistical lower limit of normal for FEV₁/VC and not per cent of predicted or fixed ratio to diagnose obstructive abnormalities is one of the real advantages of these guidelines. It will reduce the number of false-positive diagnoses as compared with using the Global Initiative for Chronic Obstructive Lung Disease or ERS/ATS COPD guidelines.

It is unlikely that a single interpretive strategy will work for all patients at all times, given the diversity of respiratory disorders that may be encountered. Likewise, persons with responsibility for the interpretation of spirometric tests must recognise this fact. Furthermore, it is our expectation that those who interpret spirometry tests have appropriate training and experience to do so. These guidelines are not "cookbooks".

While manufacturers may use our guidelines as a basis for computer interpretation of results, all tests should ultimately be read by appropriately trained personnel.

We hope the readers of the recent American Thoracic Society/ European Respiratory Society guidelines on lung function will agree that it represents a general consensus even though it was not unanimous. We are confident they will understand that it is only with an integrated interpretation of clinical and functional data by physicians that we may be of help and not harm to our patients.

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Risk factors of frequent exacerbations in difficult-to-treat asthma

To the Editors:

We read with interest the recent paper by TEN BRINKE *et al.* [1], which describes the prevalence of comorbidities in “difficult-to-treat” asthmatics and the association with recurrent exacerbations. This adds to other papers examining these factors in similar populations but reached some differing conclusions, which we felt merit further discussion.

The study involved 136 patients initially; however, only 63 patients were included in the main analysis. A total of 54 patients were excluded because of their continuous use of oral steroids as the authors reported that defining an exacerbation was difficult in this group. We are unclear why this could not have been defined as the requirement for an increase in oral steroid above the usual maintenance dose. This would have increased the number of patients in the study and included those with more severe disease. The reader can only assume that the remaining 29 patients are those with two exacerbations in a year and, thus, the “study population” of 136 seems a little misleading, and rather selected, when the number of subjects analysed was 63.

The definition of difficult-to-treat asthma was made on the basis of treatment requirements and persistent symptoms. Two published systematic evaluation protocols, performed independently in populations defined in this way, have shown that a significant proportion of patients have unidentified or alternative diagnoses [2, 3]. When these are identified and managed, it results in a significant proportion of these patients becoming straightforward to manage [2, 3]. If this important differentiation was not made prior to this study, then a significant proportion of patients entered in this study may not have had persisting symptoms due to asthma.

Another issue, which does not seem to be addressed, is poor adherence. Both recent systematic protocol studies in difficult asthmatics assessed adherence to systemic steroids, and found that 32% [3] and 56% [2] were nonadherent. Using 6-monthly prescription refill records, 45% of patients attending the Belfast Difficult Asthma Clinic (Belfast, UK) were filling <50% of their prescribed combination inhaler (personal communication, J. Gamble, A. Lazenbatt, L.G. Heaney, Regional Respiratory Unit, Belfast City Hospital, Belfast, UK), despite reporting they