To the Editor:

We commend CHUNG *et al.* [1] for their effort on consolidating recommendations for severe asthma in the European Respiratory Society/American Thoracic Society guidelines on the definition, evaluation and treatment of severe asthma. However, we were concerned by the recommendation that bronchial thermoplasty be performed "only in the context of an Institutional Review Board-approved independent systemic registry or a clinical study" [1]. In addition to the positive benefits observed in our patients, bronchial thermoplasty has been demonstrated to be effective in several studies, including the pivotal AIR2 (Asthma Intervention Research 2) trial which resulted in this therapy's approval by the US Food and Drug Administration in 2010 [2, 3]. It has been shown to improve asthma-related quality of life and reduce exacerbations, emergency room visits and hospitalisations. Furthermore, these benefits have been sustained for >5 years with no significant safety concerns [4, 5]. We agree that it is important to monitor the efficacy and safety of this and other new therapies in the real world, and that studies to better understand phenotypes of responding patients are warranted. However, mandating that this therapy be limited to the research setting will prevent many patients suffering from severe asthma with ongoing unmet needs from gaining access to bronchial thermoplasty and gaining better control of their disease. Given the demonstrated long-term efficacy (>5 years) and safety of this therapy, and since the therapeutic options for patients with severe asthma are currently limited, we feel that it is important to include bronchial thermoplasty for consideration as an effective treatment option for patients with severe refractory asthma.

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Bronchial thermoplasty is a safe and effective therapy for patients with severe, refractory asthma
http://ow.ly/vhgS0

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From the authors:

We thank David L. Hahn, and Michael E. Wechsler and Gerard P. Cox for their letters and for the points they have raised.

In relation to Dr Hahn's comments on the macrolide antibiotics we stress that a systematic review was performed, but focusing on studies that included patients with severe asthma. The study by BRUSSELLE *et al.* [1] should have been included but it had not been published at the time we performed the analysis. Inclusion of this study would have provided more data about asthma control and quality of life; however, its results were consistent with the results of the already included studies and would not change the estimates and the recommendation. The choice for the four studies that we analysed is fully described in the text. The guideline panel felt that there was a real risk of developing bacterial resistance to prolonged macrolide therapy, as shown in the recent studies referred to by Dr Hahn [2, 3]. Although the potential harm that this bacterial resistance

could represent in these patients is unclear, the panel felt that it was quite reasonable to take a cautious approach here, balancing these potential risks with the potential benefits of this therapy.

Dr Wechsler and Dr Cox question the recommendation that bronchial thermoplasty be performed ''only in the context of an Institutional Review Board-approved independent systematic registry or a clinical study'' [4]. The background to this decision is made explicit under the sections ''Values and preferences'' and ''Remarks'' with the uncertainty of the net benefit from using bronchial thermoplasty in patients with severe asthma and the need to evaluate long-term effects of this procedure in these patients. In addition, determining the type of patient with severe asthma who would benefit from bronchial thermoplasty is another important issue that needs to be addressed. The paper mentioned by Dr Wechsler and Dr Cox [5] that reports on the long-term safety and effectiveness of bronchial thermoplasty was published after we had completed our analysis. It contains important safety data on the 5-year follow-up of 85% of asthma patients treated in the AIR2 (Asthma Intervention Research 2) trial.

We do not believe that this recommendation should limit access to bronchial thermoplasty. The guideline panel felt that bronchial thermoplasty was a relatively new and promising intervention associated with the potential appreciable harm and cost. The guideline panel was concerned at providing a premature favourable recommendation for the use of bronchial thermoplasty in severe asthma, encouraging the rapid diffusion of the intervention associated with an uncertain balance of benefits and harms. The guideline panel was equally reluctant to recommend against using thermoplasty until more data became available, with the disadvantage that this could inhibit further investigation. By making a recommendation to use bronchial thermoplasty the data concerning its benefits and safety could be systematically collected and, in doing so, it was intended that this would stimulate efforts to answer the remaining questions related to this new treatment. The guidelines provide detailed suggestions about the specific research questions that should be addressed, particularly in which patient important outcomes should be measured.

Evaluation of treatments for severe asthma remains a difficult area but the explicit and transparent GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach in this context is useful, achieving a balanced recommendation of the benefits and harms of these treatments that is understood by both patients and clinicians.

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Clarification of recommendations for the uses of macrolide antibiotics and bronchial thermoplasty for severe asthma http://ow.ly/wRV6B

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