

## Correspondence

**Questioning the economic evaluation of omalizumab**

*To the Editor:*

Developing clinical and economic models for estimating the cost-effectiveness of new medical therapies is challenging and often requires selecting and synthesizing information to construct a simpler approximation of clinical reality. We appreciate the efforts of Wu et al<sup>1</sup> in helping to articulate the factors involved in understanding the cost-effectiveness of omalizumab in the treatment of patients with severe asthma. However, we think that the current model structure and assumptions might not completely capture the outcomes and costs of clinical practice with omalizumab. Our main concerns are about the quantification of the quality-of-life benefits, the structure of the model, and the focus on FEV<sub>1</sub> as the main outcome measure.

Asthma is recognized as an airway inflammatory disease, and new treatments target the cellular and molecular mechanisms regulating this inflammation. Omalizumab is a recombinant humanized anti-IgE antibody.<sup>2</sup> Although the mechanism by which an anti-IgE might improve asthma control remains uncertain, it clearly does not have any bronchodilating effect and might be viewed as a selective bronchoprotecting agent against airway reaction elicited by an allergen.<sup>3</sup> The Asthma Policy Model bases quality-of-life benefits on effects on pulmonary function that might be reasonable for economic evaluations of bronchodilator therapies but might be inappropriate for omalizumab. In addition, there is only a moderate (at best) association between pulmonary function and quality of life and symptom experience in asthmatic patients. Therefore the current model might underestimate the effectiveness of omalizumab on quality-of-life outcomes. A recent meta-analysis of quality-of-life outcomes across 5 omalizumab clinical trials clearly demonstrates a 1.6- to 2-fold increase in moderate and a 1.8- to 2.1-fold increase in large improvements in Asthma Quality of Life Questionnaire overall scores for the omalizumab-treated versus the placebo-treated groups (combined with standardized inhaled corticosteroid regimens).<sup>4</sup> These findings seem at odds with the modest improvements in quality-of-life outcomes included in the Wu et al<sup>1</sup> model.

The assignment of health preferences to changes in pulmonary function is not supportable given the expected minimal effect of omalizumab on FEV<sub>1</sub> measurements because of the drug's mechanism of action (see above). Although these authors recognize that preference-based and psychometric-based quality-of-life measures are not closely related,<sup>5</sup> they nonetheless use an estimation method that certainly underestimates the quality-of-life benefit of omalizumab treatment. Again, this assumed relationship between pulmonary function and health preferences seems likely to underestimate the effect of omalizumab on quality-of-life outcomes in asthmatic patients. Because adequately quantifying the "effectiveness" of a treatment is essential for a cost-effectiveness analysis, the methods used by the authors seem unlikely to capture the complete benefits associated with omalizumab therapy.

The model used for the analysis was published previously<sup>6</sup> and appears to be robust in estimating the effect of educational and

therapeutic interventions in patients with mild persistent and moderate asthma. The efficacy of therapies can be followed by using changes in incidence of exacerbations, resource use, and FEV<sub>1</sub> increases. We agree with their use of these measures for treatment efficacy, but as noted above, changes in FEV<sub>1</sub> in the chronic persistent allergic asthmatic population is not a sensitive measure. The Asthma Policy Model was designed to analyze inhaled corticosteroid therapies and might not capture the extent of improvements in this population with severe allergic asthma managed with olamizumab.<sup>6</sup>

Wu et al<sup>1</sup> mistakenly comment that Brown et al<sup>7</sup> only focus on omalizumab responders to obtain an attractive cost per quality-adjusted life year. Our analysis studied the costs and outcomes associated with all patients who were considered to meet the Global Initiative for Asthma moderate-to-severe patient category enrolled in the clinical trial. In our model the patients with severe-to-moderate disease not responding to omalizumab treatment were switched to inhaled corticosteroid best supportive care after 16 weeks, according to the European treatment label. It is difficult to reconcile that a physician would continue treating a patient who can be shown as not responsive to therapy. Maintaining non-responding patients on omalizumab therapy certainly contributes to the estimated high cost-effectiveness ratio obtained in the Wu et al<sup>1</sup> analysis. Combined with the underestimation of quality-of-life benefits, this cost-effectiveness analysis might not adequately reflect the overall medical costs and outcomes of omalizumab therapy in patients with severe allergic asthma.

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