LETTER TO THE EDITOR

Comment on: “Cost Effectiveness of Tiotropium in Patients with Asthma Poorly Controlled on Inhaled Glucocorticosteroids and Long-Acting β-Agonists”

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Dear Editor
Re: Willson et al. [1]

1 Introduction
When performing a re-analysis of our study data, we found an error in the calculation of the transition matrices in our published analyses relating to how patients’ asthma-control states at weekly study visits had been imputed and subsequently used in our original model. We have therefore re-analysed the data using revised transition matrices and also performed additional sensitivity analyses to confirm the reliability and validity of the conclusions.

2 Re-Analysis of Study Data
The original Bayesian biphasic model was based on the observed number of weekly patient transitions in the clinical trials using six-question Asthma Control Questionnaire (ACQ-6) results and suggested that, in both treatment arms, there was a rapid improvement in the number of patients who were considered to have both controlled and partly controlled asthma in weeks 1–8, followed by a slower rate of change in weeks 9–48. The re-analysis of study data using the revised transition matrices predicted that tiotropium add-on therapy reduced exacerbations and improved asthma control with an incremental cost-effectiveness ratio of £28,383 (obtained at 2012 prices) per quality-adjusted life-year (QALY) gained, which is within the commonly accepted £20,000–£30,000 per QALY gained willingness-to-pay threshold used in the UK [2]. There was a 52 % likelihood of cost-effectiveness at a willingness-to-pay of £30,000 per QALY gained and a 31 % likelihood of cost-effectiveness at a willingness-to-pay of £20,000 per QALY gained, when compared with usual-care treatment.

Although this re-analysis resulted in a higher overall incremental cost-effectiveness ratio, tiotropium was still found to be cost-effective when added to usual care in patients whose asthma remained uncontrolled despite treatment with high-dose inhaled glucocorticosteroids (ICSs) with long-acting β2-agonists (LABAs) (budesonide 800 μg/formoterol fumarate 24 μg or fluticasone propionate 500 μg/salmeterol 100 μg), in line with the overall conclusions from our original publication. However, this result was associated with greater uncertainty, reducing the likelihood of cost-effectiveness at a willingness-to-pay of £30,000 per QALY gained from 66 % to 52 %.

3 Additional Sensitivity Analyses
To address the increased uncertainty, we performed additional sensitivity analyses to explore the robustness of the revised model.

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The original model used a biphasic approach with different transition matrices for weeks 1–8 and 9–48. The results of the re-analysis of study data suggest that this approach may have underestimated the early treatment effect and overestimated the late treatment effect. We have therefore performed additional sensitivity analyses using a number of modelling approaches including a Bayesian monophasic model, a hybrid model which combines a biphasic approach for the asthma-control states and a monophasic approach for exacerbations, and a model using tunnelling states. We also examined whether the ACQ version [ACQ-6 or seven-question ACQ (ACQ-7)] affected the results (Table 1).

The results of these additional sensitivity analyses show that tiotropium may be cost-effective when added to usual care in patients whose asthma remains uncontrolled despite treatment with high-dose ICS plus LABA, irrespective of the modelling method used, and so provides additional confidence that the conclusions presented in our published manuscript are valid.

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