Author's response to reviews

Title: Rational Choice of Cholinesterase Inhibitor for the Treatment of Alzheimer's Disease in Canada: A Comparative Economic Analysis

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Responses to Reviewer Comments

Rational Choice of Cholinesterase Inhibitor for the Treatment of Alzheimer’s Disease in Canada: A Comparative Economic Analysis (MS: 1280700189193396)

Major Compulsory Revisions

1. Table 3 Lacking

Table 3 was accidentally omitted and has now been reinstated.

Minor Compulsory Revisions

1. What are the confidence intervals for the coefficients used in the equation to forecast cognitive status?

   The confidence intervals have been added to the text.

2. Is the fact that the utility for FTC is equal regardless of location based on an assumption?

   The source study for our utility estimates found that setting of care was not an independent predictor. Text explaining this has been added to the manuscript.

3. Add decimal places to 21 and 36.

   Decimal places have not been added to these figures because it makes more sense to us to accord with the discrete nature of the ADAS-cog scale.

4. Treatment efficacy: ITT analysis=true ITT or LOCF? Need to explain the implications of this.

   Treatment efficacy was based on ITT with LOCF. Text has been added to the manuscript to this effect.
5. Provide an example of how the base likelihood of withdrawal is adjusted for treated patients.

An example has been added.

6. The daily cost of cholinesterase inhibitors was the same for all. Flat pricing was used, regardless of dose?

Yes. Flat pricing is currently in place in Canada (cost independent of dose, within recommended dosing regimens). A note to this effect has been added to the text.

7. Explain what happens if a patient stops treatment after 6 months.

Treatment discontinuation prior to needing FTC was not considered, although one might expect that in addition to no longer incurring treatment costs, benefits attained through treatment prior to discontinuation may be lost over time. Text to this effect has been added to the manuscript.

8. Add the cost/QALY for the case where galantamine was $3 more expensive.

Done

9. What was the range used for health utilities in the sensitivity analysis?

These were varied by 25% in either direction. This is now noted in the manuscript.

**Discretionary Revisions**

1. Needs a little bit more transparency? Is it a Markov model? What is the relation between ADAS-cog and FTC?

The AHEAD model has been described in detail elsewhere (Caro et al., Neurology 2001;57:964-971) and was not included except in overview in order to keep the paper focused. The methods in this paper focus instead, on derivation of the model inputs for the comparative analysis. The introductory paragraph of the methods has been modified to clarify the model structure and methods used.
2. How can the drug have an affect on cognitive symptoms and have an effect on FTC, but not on survival?

As there is no evidence to date that cholinesterase inhibitors improve patient survival, we took the conservative approach and did not assume that changes in cognition would influence survival. The last paragraph in the Treatment Efficacy section has been expanded to detail this aspect of the methods.