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## Response to Abid Iraqi and Terry L Hughes

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### To the Editor

We appreciate the interest of Drs. Iraqi and Hughes in our study entitled “Risk of Pneumonia in New Users of Cholinesterase Inhibitors for Dementia”. Their comments mainly concern the residual confounding by severity that resulted from the labeled indications of donepezil. Although we used multivariable adjustment and high-dimensional propensity score estimation to minimize the confounding effects, the residual confounding by severity is possible. However, we considered the confounding effect to be relatively small when compared among users of cholinesterase inhibitors because prescribers may pay much more attention to patients’ situations such as tolerability of medication and comorbidity when choosing a cholinesterase inhibitors rather than the labeled indication relative to severity.

We found the use of antipsychotics was associated with risk of pneumonia by multivariable Cox proportional hazards model. Our explanations were that the mechanism of action on neurotransmitters of antipsychotics could lead to higher risk; and also antipsychotic use may be a surrogate for more severe dementia. The second concern of Drs. Iraqi and Hughes was that antipsychotics may not be a surrogate for more severe dementia because Parkinson may cause psychosis as well. However, psychosis in Parkinson disease was not sufficient to account for the difference because it could occur regardless of the severity of dementia and its incidence rate has been reported to be relatively rare (79.7 per 1000 person-years).<sup>1</sup>

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Moreover, we adjusted for Parkinson disease as well as Lewy body disease by regression model.

As to their final comment, we appreciate Drs. Iraqi and Hughes highlighting the availability of once-daily galantamine since 2004 in the US. Additionally, we offer that the proportion of users of twice-daily galantamine was 86% versus only 14% once-daily in the study, which indicates the majority of physicians considered twice-daily formula of galantamine.

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## REFERENCES

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