Author’s response to reviews

Title: Potential cost savings to be made by slowing cognitive decline in mild Alzheimer's disease dementia using a model derived from the UK GERAS observational study

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Dr Tovah Aronin
The Editor
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Dear Dr Aronin

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Potential cost savings to be made by slowing cognitive decline in mild Alzheimer’s disease dementia using a model derived from the UK GERAS observational study

On behalf of my colleagues, I would like to thank the reviewers and yourself for your assessment of our manuscript as potentially acceptable for publication. We have addressed the requested
Editorial revisions within the manuscript, and include below our responses in this letter on a point-by-point basis.

I thank you for your time in reviewing our submission and look forward with interest to the journal’s review of our updated manuscript. All correspondence should be directed to me (the corresponding author) at the above address.

Yours sincerely

Alan Lenox-Smith FRCP FFPM
Corresponding author

Reviewer 1

a) Comment: The notion that slowing cognitive decline will entail cost savings appears intuitive; however, establishing a valid quantitative estimate of the savings is largely impossible given the available data (not just in GERAS, but in economic evaluations in general).

Response: We thank the reviewer for this thought-provoking comment. Whilst we acknowledge the difficulties in establishing potential savings, we believe that the GERAS data do uniquely enable us to give an estimate of the potential savings. This is particularly true due to the prospective nature of the GERAS study design. We have included additional information within the Background section (Page 5), acknowledging the paucity of data to clearly demonstrate any potential savings associated with slowing cognitive decline in AD. It is hoped that this analysis may raise awareness amongst those working in the field of the need to attempt to further elucidate exactly how great those potential savings might be. As noted in the Discussion (Page 15), there is no established method for the assessment of cost savings, therefore, this is one approach that could be used and we believe that it is an appropriate strategy given the available data.

b) Comment: Regarding this study, the GERAS participants come from a highly select group of participants whose resource utilization may well be different from the average person with AD. Thus, the estimated cost savings reported in the manuscript are unlikely to reflect the true cost savings in the UK population.

Response: GERAS was an observational study with minimal inclusion / exclusion criteria in order to represent the “average person with AD dementia” in the community, where the majority of UK patients with mild AD dementia are treated. We acknowledge in the Discussion (Page 15) that patients needed to have a caregiver and may not be representative of all AD dementia patients, but we would assert that the cost savings noted in the manuscript would be close enough to the “true cost savings” to be meaningful.
c) Comment: Given differences in healthcare systems across jurisdictions, the study's quantitative results will also be of limited applicability to other European countries, Australia, the United States, or Canada.

Response: We would agree that this paper is only directly relevant to the UK. However, it should be noted that GERAS data are available for additional countries within Europe and so it should be possible to conduct similar analyses to examine potential cost savings in these other countries.

d) Comment: The full cost question is not considered in the manuscript because moderate and severe persons with AD are omitted from the analysis; also, the time horizon is limited to 18 months, which is far short of the average time from diagnosis to death in persons with AD.

Response: We never attempted to look at the potential savings that could be made in all patients with dementia, but, as in the title, have concentrated on those with mild dementia, who form the population being targeted for treatment in the majority of current clinical trials. Moreover, these individuals were chosen due to the assumption that that they represent the group most likely to substantially reduce their other healthcare requirements if their rate of cognitive decline is slowed [Williams and Kemper, J Psychosoc Nurs Ment Health Serv. 2010 May; 48(5): 42–51.], and as such will be best positioned to continue to lead a relatively normal life. For additional clarity we have added an extra sentence in the Discussion (Page 16) emphasising that this is a potential limitation. Regarding the 18-month timeline, we fully accept that this is a limitation and refer to this in the Discussion (Page 16). However, the data up to 18 months are, within reason, robust, which is why we have published them first. It is our intention to look at the longer term in the future, but this will include further assumptions and thus be less robust than the data presented in the current paper.

e) Comment: In the discussion, the authors mention the potential advantages of early treatment in persons who are at risk of dementia (prior to diagnosis!) (p. 14, lines 39-44). The evidence for the efficacy of early treatment, especially prior to diagnosis, is quite weak and the authors should acknowledge this point in the discussion (or, better yet, remove this content from the discussion entirely).

Response: We agree that the evidence for this is weak and have deleted this paragraph as suggested.

f) Comment: The methods do not clearly describe the valuation and calculation of societal costs, nor do the results provide any details of the participants' resource utilization. Overall, the resources and costs take on a bit of a 'black box' quality in how they are reported in this study.

Response: More complete information on the valuation and calculation of societal costs, as well as resource utilisation is given in the first paper (BMC Geriatrics 2016;16:195). We have modified the Methods section (Page 8) to reference this more clearly.

Reviewer 2
g) Comment: it is not clear to me that the study includes the costs of pharmaceuticals. While table 1 lists the percent users of acetylcholinesterases and memantine, the section on data collection does not indicate that the costs of these drugs are included in the analysis. I think this is important, since the incremental cost savings indicated in the study are modest, and on an annual basis are not significantly different than the cost of these medications.

Response: The study did include the cost of acetylcholinesterases and memantine. This is in the original paper referenced in response to point f) and, as previously, we have now referenced the first paper more prominently (Page 8) so that further details on the methods can be found. We agree that the cost savings are modest, as acknowledged on Page 13 of the manuscript. The main reason for this is believed to be the slow progression from mild to moderate disease that was observed over an 18-month time period.

h) Comment: Most of the newer disease modifying drugs being tested or anticipated will cost far more than the cost savings predicted by the modelling studies presented here.

Response: The cost of new drugs is a complex issue (and unknown at this point) and we believe that this manuscript is not an appropriate platform for this discussion, although our paper does contribute information of relevance to further discussions when such drugs are available.