Reviewer's report

Title: Using an onset-anchored Bayesian hierarchical model to improve predictions for amyotrophic lateral sclerosis disease progression

Version: 1 Date: 04 Dec 2017

Reviewer: Brian Smith

Reviewer's report:

The authors are commended for their thoughtful and thorough responses, and revisions made to their manuscript. The main issues raised in my original comments and suggestions have been satisfactorily addressed. The substantial changes and efforts have strengthened what had already been a very strong manuscript. I only have two general follow-up comments to ones made previously.

1) MSE and DIC are metrics used appropriately in the manuscript to compare fits of competing models. However, comparing model fits is different from checking the fit of a model, including its distributional assumptions, to the data. For example, one model may fit better than another according to DIC, but both may produce replicate data that are dissimilar from the observed data. Model checking, rather than comparison, was the intended suggestion in my original comment concerning posterior predictive p-values. The authors do provide posterior distributions and credible intervals to check the fit of predicted to observed ALSFRS values (Figures 4 and 5) which can be viewed as posterior predictive model checks and as addressing my original comment.

2) The authors note the large variances of their inverse-gamma prior distributions as the reason for referring to them as "uninformative". Even with large variances, such priors can have strong influences on posterior inference as discussed and illustrated in a 2006 Gelman paper. That paper has been widely cited and is growing in familiarity among readers/reviewers. In it, Gelman goes so far as to recommend against the use of inverse-gammas for variance parameters in hierarchical models, as are the ones specified in this paper. I am not suggesting that the authors make this or other changes to their analysis, but again offer a word of caution about using the term "uninformative" particularly for their variance priors.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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