Author's response to reviews

Title: An exploration of the association between very early rehabilitation and outcome for the patients with acute ischaemic stroke in Japan: a nationwide retrospective cohort survey

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Author's response to reviews: see over
Dear Reviewers and the Editorial Office

We would like to express our sincere appreciation for additional comments from Drs. Lindeman and Leathley. We follow their advices and prepared second revision as follows.

**Comments from Dr. Eline Lindeman:**
1. *Page 4.* Stating that Bernhardt defines VEI as a start within 2 days needs a clarification why in the present article VEI is defined as a start within 3 days. Maybe you should remove the VEI definitions in the introduction and shortly discuss the broad scope in the discussion section.

   Following your advice, we removed the sentence from the introduction, and moved it to a study limitation part of the discussion section.

P20 L17 (discussion, study limitation part)
Revised: Due to a lack of information on hourly period and details of the rehabilitation therapy, we defined in this study VEI as intervention commencing within 3 days after admission, which may prohibit simple comparison of our findings with those in previous studies. Bernhardt et al. defined VEI as intervention commencing within 48 hours after stroke onset [6,7]. They also considered VEI to be any intervention delivered with the aims of reducing the time from stroke onset to first mobilisation and increasing the amount of out of bed physical activity [6,7]. Further investigation may be necessary with the standardized definition of VEI.

2. *Page 6.* 5th sentence from below: Replace ‘The authors used the day of ….’ By ‘We used the day of ….’ (to prevent the suggestion that McGuire used the day of …)
   We apologize for unclear description of the sentence. By “The authors” we meant McGuire, et al. They used the day of admission as an instrumental variable. To avoid confusion, we revise the sentence.

   Original: The authors used the day of admission,
   Revised: McGuire and colleagues used the day of admission.

3. *Page 7.* Remove ‘such as the US Medicare claims database or the US Nationwide Inpatient Samples’
   Following your advice, we removed the description.
4. Page 21 and start 22. In my opinion no ‘new data’ should be introduced in the discussion section: Suggestion to shorten the text:

Following your advice, we revised the description as follows.

Revised: Due to voluntary participation, there might be a possibility of sampling bias. We compared hospitals who submitted both claim and clinical data (and were included in the analysis, N = 294) with those who submitted claim data only (N = 681). Patient mortality was relatively higher in the excluded hospitals (3.6% vs. 4.8%, p < 0.001), and average age was older in the excluded hospital (72.1 vs. 72.7, p < 0.001). There was no difference in gender composition. The average size of the included hospitals was slightly larger than that of the excluded hospitals. Most prominent difference was that in general, included hospitals were more likely to be high-volume large general hospitals specializing in acute care of stroke while the excluded hospitals were more likely to be smaller private facilities providing a mix of acute and chronic care services. Thus, the presented results in our analysis may be applicable only to the larger acute hospitals, and whether VEI exhibits a similar effect on patient functional outcome in a broader range of hospitals needs further investigation.

5. Page 22 Because in my opinion no ‘new data’ should be introduced in the discussion section I suggest to remove: ‘We conducted a sub-analysis by hospital and preliminarily found that the average functional outcomes in those hospitals with relatively low training intensity tended to be worse than in those hospitals with higher intensity treatment, even after adjusting for the functional severity of patients at admission (data not shown)’. Showing these data to the reviewers was sufficient in my opinion.

Thank you for your advice. We removed the sentence.

6. Figure 1 comes outside the page margins.

Our apologies. We checked the layout of the figure.
Comments from Dr. Leathley

The word effectiveness is still in the title, I would prefer it if this could be altered to something along the lines of “An exploration of the association between very early rehabilitation and outcome for ...” particularly because this is how the aim is written in the second sentence of the Background.

Following your advice, we revised the title as follows.

Original: The effectiveness of very early rehabilitation for acute ischaemic stroke patients in Japan: a nationwide retrospective cohort survey

Revised: An exploration of the association between very early rehabilitation and outcome for the patients with acute ischaemic stroke in Japan: a nationwide retrospective cohort survey

Related we also revised the last sentence in the introduction as follows;

Original: Using a larger observational dataset and proper statistical methods such as IV would, therefore, allow us to determine the effectiveness of VEI treatment, which shaped the purpose of this study.

Revised: Using a larger observational dataset and proper statistical methods such as IV would, therefore, allow us to determine the association of VEI treatment with patient’s outcome at discharge, which shaped the purpose of this study.