Comments to the Authors,

This study conducted by Dr. Hermann Brenner deeply investigated the relationship between DNA methylation age acceleration, frailty and telomere length. The result shown the age acceleration is significantly associated with a comprehensive frailty measure but no correlation was found between age acceleration with telomere length. The study was performed rigorously and the findings sound greatly interesting. What’s more, it would be an exciting example to clarify the correlation between epigenetic age and telomere length with frailty related complex phenotypes. However, I only have several concerns to make the manuscript more solid. In general, I'd recommend publication if the authors can address the following concerns and prepare a more concise draft.

Major Compulsory Revisions

1, In the Table 1, the difference in the main characteristics should be tested between the dataset1 and dataset2 and provided the P-value.

2, In the method section of Epigenetic age and age acceleration, the DNA methylation age were predicted by the fixed model of Horvath 2013, or the model trained by your own dataset?

3, The PCA analysis based on 353 loci should be conducted in dataset1, dataset2 and integrated dataset to check the batch effect. And the results should be provided as the supplementary Figures. Batch effect analysis in Clinical Epigenetics 2015, 7:3 shown that it would influence the data structure deeply.

4, the result “Age acceleration and telomere length are not correlated” could be expected theoretically. The author can try to test the correlation between TL with age as well as methylation age, respectively. Then compare the difference between these two prediction models? For example, which one is better?

5, In the Table 4, I can understand to check the correlation between TL and FI in different meth-age group. However, why not take TL and methylation age acceleration into the linear model simultaneously? What’s more, in the result section of “Interaction analysis of methylation and telomeres on frailty”, we can find that TL is not significantly associated with FI, is it conflict with previous studies?

6, The conclusion that age acceleration is associated with frailty is concluded using the total samples from cohort 1 and cohort2, but in the subset analysis shown in Table 3, the correlation in males of dataset1 and females of dataset 2 are not statistically significant. How to explain the inconsistent results in the subset analysis?   
7, The finding of this study would be greatly contributed to the epigenetic epidemiology research, hope more detail data can be open to the public so that further study or design can be conducted, such as the methylation level of 353 in all the samples.

**Minor Revisions**

1, The summarization of the study were not comprehensive for the abstract. Actually, Clinical Epigenetics allowed as long as 350 words in the abstract. More information could be provided in the abstract, such as which confounders? The basic study design and method? P-values? More details in the abstract could help readers to get the point quickly.

2, The citation style should be revised which is not fit to Clinical Epigenetics.

3, Please check the line from 51 to 59 in Page 6: “For example, the estimate in the age-, sex- and leukocyte distribution-adjusted model was -0.0004 instead of -0.0006, the result in the model additionally adjusted for cancer history was -0.0004 instead of -0.0006 (details not shown).” Is this a mistake repeat for these two values?

4, In the line 21, page6, FI increased by about 0.25 percent points per year of epigenetic age acceleration, which—since the FI used increases by about 2.9 percent points per deficit—translates into one additional deficit per 11.6, or roundabout half an additional deficit per 6 years of age acceleration, respectively. I got the author’s point, However, I think, the representation should be more clear, with short and explicit way. But the way, the way how the 6 year were calculated should be give more interpretation.

5. In the line 23, page 7, I think roundabout should be “round about”?