Author’s response to reviews

Title: Nepal Pioneer Worksite Intervention Study to Lower Cardio-metabolic Risk Factors: Design and Protocol

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Author’s response to reviews:

I am extremely pleased to resubmit a revised version of the manuscript titled "Nepal Pioneer Worksite Intervention Study – Design and Protocol". I highly appreciate the time and effort provided by the reviewer and the editor. I have incorporated the suggested changes into the manuscript to the best of my ability. Append to this letter is our response to the comments raised by the reviewers. As you will notice, we agreed with all the comments raised by the reviewers. Accordingly, we have uploaded the revised manuscript.

Editor Comments:

1) In the trial registration statement after the abstract, please include the date of registration.
We added the date of registration

2) In the Funding section, please remove the last sentence.

We removed the last sentence

3) Supplemental files 2 and 3 can be removed as these are no longer needed.

We removed the files.

Reviewer reports:

Michael Wirth (Reviewer 1): I thank the authors for considering my comments. I read the paper again and did not have any edits or comments to suggest to the text changes. However, there are just a couple of issues that I think are really important for the researchers to consider or at least note in the manuscript. I would like to note that my comments aren't just for critiquing the work, but also so that these important details can be added to the manuscript for other researchers. I am sure you would like to collaborate and have other researchers reach out to you to collaborate on analyses. Having information related to my comments may help facilitate that.

We appreciate your comments and they have helped the paper be more clear.

1. Related to the measurements of biological markers of shift workers, I think you should explicitly state that you will record the time of blood draw and have an indicator for the most recent shift worked prior to the blood draw. This will help readers and potential collaborators understand that these measures can be adjusted for to control the effect of circadian rhythms of the blood measures.

We have added that in the “Laboratory” subheading of the Methods section.

2. I think you should consider adding a statement that assumptions of the statistical tests will be examined and if violated non-parametric testing can be explored. I understand that the t-test will provide the same effect size even if the distribution is non-normal, the same would be true for the regression. However, this will affect your variance, and, in turn, your ability to detect a statistically significant finding. I understand that your power is based on using t-test. The problem is that one can power a study on a specific test all day long, but at the end of the day, if the assumptions of that test are violated, it still isn't appropriate to use that test. I am more concerned with the linear regression. Normality of the residuals is just one of the assumptions. Violations of homoscedasticity, in my opinion, are even more concerning for power. Although I do not live on p-values and
prefer effect estimates, the analyses still need to fit the data. Linear regression is actually quite robust. In fact, many researchers do not realize how robust it is and you will probably be fine given the sample size. However, preliminary work that I was involved in showed that with a skewness of model residuals of 6.0 and a large sample size, linear regression is still feasible. However, after a skewness of about 3, linear regression actually becomes less powerful than quantile regression. So, if you powered your study assuming the assumptions of these tests are upheld, and in fact they aren't, then you may not have the power to detect statistically significant results. Or, it could be that other tests are actually more powerful and better fit the data structure. That long diatribe was just to say that you should mention that you are open to considering other analytic techniques if assumptions are not upheld.

Thank you for the elaborative explanation. We have added the “Data Analysis Plan” subheading of the Methods section.