Reviewer’s report

Title: Understanding the impact of five major determinants of health (genetics, biology, behavior, psychology, society/environment) on type 2 diabetes in U.S. Hispanic/Latino families: Mil Familias - A cohort study

Version: 0 Date: 23 Sep 2019

Reviewer: Xiqian Huo

Reviewer's report:

Thank you for the opportunity to review this study protocol. In this study, Dr. Morales aimed at establishing an observational cohort of 1,000 Latino families, and assessing the effects of five determinants of health on diabetes burden in US Hispanic/Latino families. I have some concerns mainly pertaining to the study design and clarity of the text.

Major comments

Comment 1: Though involving a relative large number of families in this cohort study is a strength, quality control to ensure standardisation of protocol implementation including patient selection, enrolment, and data collection become critically important. This paper should include a description on quality assurance in this study.

Comment 2: Description of outcomes needs to be clarified in a concise way. This paper should include a description on the primary and major secondary outcomes and their definitions in the methods section.

Comment 3: Prognostic outcomes are important in long-term cohort studies assessing the influence of determinants and other risk factors associations. Particularly, will the "hard outcomes" or events be collected during the study period (namely, death, diabetes major vascular complications, and micro vascular complications), and how will the events be collected and adjudicated? How about events not captured in the study hospitals? Or through self-report?

Comment 4: The study actually began in about February 2019 according to clinicaltrials.gov registry information, and it is nearly half year ago. The recruitment should have started already. Consider disclosing the timeline/progress status of the study.

Comment 5: Please provide a brief description on the pilot study that involved over 100 adult Latino individuals including the study design, results and findings.

Comment 6: Please specify how will the bio samples (e.g. blood samples, urine samples) be processed and stored in the study centre.
Comment 7: I wonder if you expect a bit too much from the patients and families population? The study aims to collect data annually on over 100 different variables during each visit and expects patients to monitor certain things (blood pressure etc). Are there any data on how long the encounter will be for each patient according to pilot study results? Most people that will enrol in the study will likely have little experience in long-term research participation and there is some research indicating that participants could be overwhelmed by the things they are asked to do. As a result, they might give up early on. Have you considered this? A streamlined study design will be much easier for the study implementation and ensure data quality.

Comment 8: Methods (statistical analysis): Please specify the statistical analysis methods and plans in the protocol (or add in appendix). The current descriptions are unclear and too vague.

Comment 9: Please acknowledge potential limitations of the study in the discussion.

Minor comments

Comment 1: Abstract: Please spell out an acronym the first time it is used (e.g. "US" in the abstract).

Comment 2: Introduction: The author explained that genetics, biological factors and society/environment influences are important factors in determining diabetes risks. How about the other two determinants (i.e. behavior and phycology influence)? In addition, the associations between many of the above risk factors and outcomes have been well studied in previous studies actually; please add statements about why the study needs to be done now and what are the gaps in existing data and evidence.

Comment 3: Introduction (Line 85-89): Definitions of the study population ("Hispanic/Latino" and "Latinos" identification) should be explained under the methods section.

Comment 4: Methods (Participants): Will there be logs of people who are not eligible or declined from the study? If so please add in the paper, otherwise please state the reason.

Comment 5: Methods (Participants): The current definitions for family representative and family members are unclear. I would suggest separate definitions for two populations, for example, clarify the inclusion and exclusion criteria for family representative first, and then explain the identification (or eligibility criteria) for family members.

Comment 6: Methods (Activity Monitoring): Why do you choose the cutoff value of 13 years old for wearable monitors? The study require the participants to wear the devices for up to a week, however, how will the study monitor the adherence of the wearable devices? How will the data be transferred to the study center (e.g. by Bluetooth?)
Comment 7: Methods (Activity Monitoring): The wearable monitor is a kind of the intervention on participants' physical activity in this observational cohort study although the concern will be alleviated since the device is only used for a week and up to twice within 12 months.

Comment 8: Methods (Statistical analysis): The author stated that given the size of the cohort, a power calculation is not required. However, sample size calculation needs to be performed previous to the study and it would be better if the authors could provide a formal sample size calculation.

Comment 9: Methods (Figure 1): It is unclear that whether the HPA encounter, laboratory encounter and questionnaires encounter are conducted at the same visit, or are there any interval requirements between these encounters. The author should clarify this in the methods text and figure.

Comment 10: Discussion (Line 335-337): Please add reference for the cited literatures.

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

No

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.

Unable to assess

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 recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
Declaration of competing interests

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

None conflicts of interest.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal