Author's response to reviews

Title: Obesity and Hypertension in an Iranian Cohort Study; Iranian Women Experience Higher Rates of Obesity and Hypertension Than American Women

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Author's response to reviews: see over
Dear Editors,

I would like to appreciate the thoughtful comments and kind compliments from the reviewers. Attached, I am sending the revised version of article based on the comments from reviewers.

The main compulsory revision asked for by reviewers were regarding the participation rates in Golestan Cohort Study. We have added the data regarding participation rate in the article (Methods section, study population, paragraph 2, lines 4-5). The design of the Golestan Cohort Study was explained in a previous article (cited in our manuscript).

I would like to use this opportunity to appreciate the time and the effort that has been spent for reviewing this article.

Point-by-point reply to reviewers (reviewers comments are in *Italic*):

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**Reviewer 1:**

*Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)*

None required

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*Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)*

Abstract, line 4: some text appears to be missing “compared age-adjusted ….”

Reply: Thank you very much for the attention. It is “compared age-adjusted ‘rates.’” We added the word “rates” to the abstract.

Please revise the reference formatting; many references are stated after the period (see for instance in the Background, lines 18 and 20). Also, there should be a space before the parenthesis (see for instance in the Background, lines 12 and 17). The text should be written in the past tense (see page 1, line 8 “estimated”)

Reply: The format changes requested are made.

In the Methods (page 2, line 5), the authors state that they included 8,999 participants, but data from 8,998 is indicated in the abstract and the results. Although the explanation is provided in the beginning of page 4, it would be easier for the reader that the authors indicate that they excluded a subject because of missing data in the Methods, not in the Results.
Reply: We added that sentence to the methods section (Methods, Study population: lines 8 and 9)

*More information regarding the height, weight, waist and hip measurement should be provided; how was the rounding performed? Were the subjects wearing light clothes? The higher waist observed in this study might be due to differences in the measurement location.*

Reply: We added these data to the Methods section (under Data collection).

*Pages 5, 7 and 8: the authors indicate that they used logistic regression for the analysis of data, but this is not reported in the Statistical Methods.*

Reply: Logistic regression is a special form of generalized linear regression, which is mentioned in the methods section. However, respecting this comment, we added logistic regression to our methods. (Methods/Statistical Analysis, paragraph 2, lines 1-3)

*References: no Journal name provided in ref. 8. In refs 18 and 19, the Journal name should be abbreviated. Ref. 24: Trabzon (uppercase).*

Reply: The changes are made.

*Discretionary Revisions (which the author can choose to ignore)*

Page 6, second paragraph, line 5: “The prevalence of obesity…”

Also page 6, last paragraph, line 10 “having high WHR…”?

Figure 1 is duplicated in the manuscript. Only the first one should be kept as its graphic quality is better

Reply: The revisions are made.

**Reviewer 2:**

*Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)*

*Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)*

*Discretionary Revisions (which the author can choose to ignore). Major comments:*
The authors should discuss about the sampling method of Golestan Cohort Study.

Reply: The second paragraph in the Methods Section/Study Population explains the sampling method. The design of the Golestan Cohort Study is explained in details in a previous article by Pourshams et al (cited in our article).

Minor comments:
1. I am not sure if it is necessary to compare the middle eastern population with Pima Indians in the US and Dutch famine in the Europe, in the first paragraph of the background section?

Reply: One of the strong hypotheses regarding the increasing prevalence of obesity in developing countries is the effect of epigenetic programming and the results of the studies on Pima Indians in the US (and comparing them to Pima Indians in Mexico) as well as the studies on the people born during Dutch famine (and comparing them to other Dutch people) provide some of the strongest natural experiments supporting this hypothesis. Therefore, the main reason for mentioning these two populations in the manuscript was the possible similarities in pathophysiology of the obesity. Otherwise, these two populations have many demographic, cultural, and maybe biological differences from this Iranian Cohort.

2. The first sentence of the last paragraph in "Background" is better to be changed as: This paper in Iran using the data from a large Iranian cohort, the Golestan Cohort Study.

Reply: The sentence is revised based on the reviewer’s suggestion.

3. The last sentence of the last paragraph in "Background" is better to be deleted.

Reply: The sentence is deleted.

4. The first title under "Methods" should be "Golestan Cohort Study".

Reply: Details of the Golestan Cohort Study were reported in a previous article. However, we have provided most relevant information regarding this study in the article.

5. The first sentence under "study population" should be: Golestan Cohort Study is a large study that is being conducted in North-East of Iran and includes 8999 people between to 75 years old.

6. The second sentence under "study population" should be changed to: The study is an esophageal cancer and the associated risk factors.

Reply: This sentence is revised.
7. The 3rd sentence under “study population” should be deleted.

Reply: The phrase is deleted.

8. The second sentence of the second paragraph under “study population” should be changed to: “to participate by attending their local health service center or the Golestan Cohort Study center for interview.”

Reply: The sentence is revised based on the reviewer’s suggestion.

9. The last sentence of the second paragraph under “study population” should be changed to: “and (2) previous history of upper.

Reply: The sentence is revised.

10. Authors may refer to JNC VII for definition of HTN in their study, instead of mentioning the numbers.

Reply: We have mentioned the definition of hypertension as it was used in our study.

11. According to table 1, the prevalence of sex in the rural area is 41.7% men vs. 43% women. What about the remaining 16.3%?

Reply: Good point! The percentages in Table 1 should be read as “41.7% of men and 43% of women were living in rural areas.”

Reviewer 3:

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Study population:

Some further discussion of the results from the Golestan area to the rest of the Iranian population needed, also in the discussion section.

Reply: The second paragraph of the Discussion section has discussed the issue of generalizability and the results of another large cohort study in Iran is compared to the results of our study. The results of these two studies are summarized in Table 4 and this table demonstrates the consistency of our results with the results of another large cohort study in the capital city of Tehran. Unfortunately, there are only few population-based large cohort studies on obesity in Iran. Also, the first paragraph of the Discussion section provides some data from other studies in the Middle East, which are consistent with our results.
How high, or low, was the participation rate? This might have implications for the risk of selection bias.

Reply: Participation rate was 75% and 62% in rural and urban areas, respectively. We have added these data to the manuscript (Methods, Study Population, paragraph 2, lines 4-5)

How was the sampling conducted? This may also have implications for the question concerning selection bias.

Reply: The sampling procedure is explained in the second paragraph of the Methods section (under Study Population) and also in a previous study by Pourshams et al (cited in the manuscript).

Statistical analysis: last paragraph on page 3 indicates that a genealized linear regression model was used to estimate predictors of BMI. Was the relationship linear, otherwise some other regression model might have been more optimal.

Reply: As mentioned in the manuscript (Methods, Statistical Analysis, second paragraph, lines 3-4), we checked for models’ assumptions, including the linearity assumption for linear regressions.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Particularly the abstract might need some further English language examination.

Reply: The abstract is revised.

Data collection: the measurement of BMI (height and weight) and blood pressure by the interviewers increases the validity of these measures. In contrast, the self report of diabetes mellitus clearly decreases the validity of that item.

Reply: This is a very valid point and we have addressed that in Discussion section (page 13, paragraph 2, lines 4-8).