Reviewer's report

Title: Weight change and incident metabolic syndrome in Iranian men and women; a 3 year follow-up study

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Reviewer: Evangelos Liberopoulos

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Overall this is an interesting observational study in Iranian subjects (n=3579). During follow-up weight gain and weight loss were associated with development or amelioration, respectively, of certain features of metabolic syndrome. Although results could be logically predicted, such studies are particularly useful as they mirror what it really happens in the community.

Major comments:

1) One major limitation is that from the original 6098 subjects only 3579 were included in this analysis. For which reason were the other subjects not included? Were there any differences in baseline characteristics between subjects included and those who were not? This is essential because there could have been selection bias, i.e. those included were more interested in their health, and therefore results may not apply to the community.

2) Page 7; definition of MetSyn: How was diagnosis of MetSyn made in the presence of drug treatment? For example, if a patient had a blood pressure of 120/80 mmHg while receiving antihypertensive medication, was this considered as a criterion for MetSyn? The AHA/NHLBI (2005) definition may be more practical in this respect.

3) During follow-up there was a paradox of decreasing values for triglycerides and blood pressure despite the increasing incidence of MetSyn. This may be explained by the increasing use of drugs for treatment of MetSyn components. Adjustment for medication use in statistical models does not eliminate this problem. Authors should provide details on medication use, e.g. how many statins, fibrates, antihypertensive and antidiabetic medications. Also, what about anti-obesity drugs?

4) Do authors have any data on new diabetes onset?

Minor comments:

1) All abbreviations should be defined when first used in the abstract and text.

2) Page 2; line 5: Which Caucasians do you mean?

3) Page 4; lines 8-9: I do not understand the meaning of this sentence (i.e. ‘mechanisms of weight change and mortality’).

4) Page 4; line 13: Please include here 2 relevant studies: a) the DPP-MetSyn analysis in Ann Intern Med and b) the FenOrli study (Filippatos et al in Curr Med
5) Page 5: How many times were subjects examined?
6) Page 7: Which were phases 1 and 2?
7) Page 8; line 17: What does ‘normal subjects’ mean?
8) Page 8; line 22: Do you mean ‘normally’ instead of ‘symmetrically’?
9) Page 9; last paragraph: does ‘high’ mean above the NCEP ATP III threshold?
10) Use of more recent references is generally advised.
11) Tables 3 and 4: a) 1st column: did they have each feature at baseline or at follow-up?, b) rest columns: number of individuals should be provided.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.