

Author's response to reviews

Title: Impact of caloric and dietary restriction regimens on markers of health and longevity in humans and animals: A summary of available findings

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Author's response to reviews: see over

Reviewer's report: 1

Title: Impact of caloric and dietary restriction regimens on markers of health and longevity in humans and animals: A summary of available findings

We thank the reviewer for the insightful and helpful comments. We have addressed these below and within the text. We believe that the changes made improve the quality of the presentation.

All changes are highlighted in green.

Reviewer's report:

This is a well written review of caloric restriction and health benefits. It compares various types of dietary restriction and also somewhat obliquely, but interestingly, the religious fasting rituals. There are no major issues with the review but the authors may wish to consider the following points

1. under protein restriction, possibly cite Simpsons work on geometric framework, protein and longevity

Excellent point and this has now been done.

2. consider discussion of CR-mimetics eg rapamycin and resveratrol - because these are alternative ways of achieving same therapeutic goals as dietary manipulation

We have now mentioned this work.

3. consider discussion of cell pathways involved eg TOR, Ins/IGF, sirt and AMPK

We understand this request and have included multiple references to direct readers to a more detailed discussion of mechanisms of action. However, we opt not to include any additional text describing mechanisms of action in the present review. Our reason is based on the fact that there are so many outcomes included with these forms of fasting, ranging from actual longevity in animals to biomarkers of oxidative stress, metabolic health, glucoregulatory healthy, inflammation, cardiovascular health, etc. If we included a mechanistic discussion of one area, we feel the need to do it for all areas. The paper would then become too cumbersome. This work has already been presented and we have included references to point readers to a more thorough discussion. We hope you understand this position.

4. in the section on religious fasts - is there any data on buddhist monks who usually only eat in the morning, a sort of half ADF

We have done a literature search on this topic but have noted no peer-reviewed reports documenting this form of fasting.

5. a table comparing the longevity effects of each of the interventions would be very useful

We understand this comment and we believe that if significant data were available for each of the fasting programs compared (caloric restriction, ADF, and dietary restriction), this would be meaningful. This is particularly true for work in humans, which is generally limited to biomarkers that might reflect longevity, rather than actual longevity itself. When comparing the

studies, the outcome measures are often few and diverse across fasting forms—at least in relation to longevity. There are biomarker specific surrogates of longevity, but these are relatively similar in outcome across different fasting modes. For these reasons we have decided to maintain the text only as a method of presenting the data, as text allows us to explain findings in more detail, whereas a table only presents a “decrease/increase” type of presentation.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare I have no competing interests

Reviewer's report

Title: Impact of caloric and dietary restriction regimens on markers of health and longevity in humans and animals: A summary of available findings

We thank the reviewer for the helpful comments. We have addressed all below and within the text. We believe that the changes made improve the manuscript presentation. **All changes are highlighted in yellow.**

Reviewer's report:

I. Major Compulsory Revisions

a. I have none to suggest.

II. Minor Essential Revisions

a. I have revisions on the level of copyediting to recommend: (1) The phrase “in regards to” should be changed to “in regard to.” I noticed this twice, once in the second paragraph of the introduction (second line from the bottom) and once in the third paragraph under the heading “Daniel fast,” second to last sentence.

This has been corrected as suggested. Thank you.

(2)The authors might consider less liberal use of dashes as punctuation. The final sentence of the second paragraph under the heading “Alternate-Day Fasting and Animals” begins with “The ability of ADF to retard or prevent altogether the development of many morbidities — including: cardiovascular disease,” The dash followed by the colon is more than is needed. It would be better to punctuate the sentence as follows: “The ability of ADF to retard or prevent altogether the development of many morbidities, including cardiovascular disease, kidney disease, cancers, and diabetes, may also explain some of the observed increases in longevity.”

Point taken and correction made.

(3) In the line immediately following the heading “Caloric Restriction and Humans,” “due to” should be changed to “because of.”

Corrected as suggested.

b. In the fourth paragraph under the heading “Alternate-Day Fasting and Humans” I question the phrase “...which consisted of either 320 or 380 kcals for men and women, respectively....” Is this correct that men got the lower calorie shake and women got the higher calorie shake? This is what the “respectively” implies.

This was our error. Thank you for pointing this out. It has been corrected.

III. Discretionary Revisions

a. Currently, much of the biomedical literature on religious fasting is, as the authors suggest, focused on the Christian and Islamic traditions and to some extent on Jewish tradition, but this neglects substantial literature on traditional medicine as practiced in Tibet, India, and China, to name three important

systems of traditional medicine. Much of the literature here is contributed by historians and anthropologists, although some biomedical studies have been done. I recommend at least mentioning the importance of religious fasting in these traditions as well as in monastic communities in many religions and suggesting that future studies should examine the effects of these religious/philosophic approaches to fasting as well.

Excellent point and this has now been done.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare I have no competing interests.