Author's response to reviews

Title: Obesity survival paradox in pneumonia: a meta-analysis

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Author's response to reviews: see over
Reviewer: Darren C Greenwood PhD.

Comments to the Author:

Major compulsory revisions:

1. There is still some language implying the associations are causal, e.g. “direction of the effect” on page 10, “inverse effect” on page 12, “protective effects” on pages 13 and 14 (the concluding sentence).

**Response:**

Thank you very much for your valuable comments on our manuscript.

We revised these sentences as the reviewer requested.

2. The search strategy is still not sufficiently detailed. It is still unclear what aspects of the publication are searched, e.g. title, abstract, or text. Synonyms are not fully exploited, e.g. another name for retrospective cohort is “historical cohort”. Wildcard characters are not fully exploited, e.g. when searching for “survive” the authors may wish to also search for “survival”, when searching for death, they may also wish to search for “deaths”. Wildcard characters can make this easier.

**Response:**

Thank you very much for your enlightening comments.

We revised the search strategy. Please see the Additional File 1.

3. New discussion that meta-analysis of cohorts are prone to the same weaknesses as cohorts, includes issues of confounding, but the authors have also mentioned selection
and recall bias. These are more commonly found in case-control studies. They are not traditionally thought of as weaknesses in cohorts, because cohort selection and exposure measurement is prior to identification of outcome.

**Response:**

Thank you very much for your suggestion.

We agreed with the reviewer and revised this sentence.

4. The forest plots still need some tidying up, e.g. there is no such p-value as p=0.000, and there is some inconsistency in how the studies are referenced, sometimes including initials and sometimes not. Actually, I have just realised that these may not be initials, but “M” for male and “F” for female? If that is the case, then the same study is included twice. This messes up the measures and tests of heterogeneity, because these two sets of observations will not be independent, because they are from the same study. Better to combine dose-response slopes for males and females first, using a fixed effect meta-analysis, before combining with the other studies. This will then mean that results in the meta-analysis and forest plots are independent, and give more appropriate estimates of I-squared and Q, and the correct degrees of freedom, for tests of heterogeneity. Similarly for the funnel plots and tests of small-study effects.

**Response:**

Thank you very much for your constructive comments.

We revised the forest plots. We combined the sex-specific RR estimates using a
fixed-effects model before combining with other studies, and also revised other parts, such as the funnel plots and tests of small-study effects.

Minor essential revisions:

1. The methods section is still somewhat confused, in that the paper by Orsini et al. implements the methods proposed by Greenland and Longnecker, providing the Stata commands that the authors have used. But the methods section seems to suggest that these are two different methods. Maybe what they mean is that first they derived the linear dose-response (cite both papers) and then combined them using a (random-effects) meta-analysis.

Response:

Thank you very much for your comments on our manuscript. In this revision, we re-wrote the Statistical Analysis section.

2. Some issues of spelling and grammar remain. The most prominent being “underling causes” on page 13.

Response:

This manuscript has been edited and proofread by Medjaden Bioscience Limited again. In addition, we checked the spelling and grammar carefully.

Discretionary revisions:

1. I’m personally still not convinced by the clever mechanisms suggested to explain
the paradox. I think it’s probably just an artefact of data collection.

**Response:**

Thank you very much for your valuable comments.

We agreed with the reviewer that maybe it was an artefact. Therefore, additional prospective studies with adjustment for more confounding factors are warranted before a conclusion can be drawn.

Thank you very much again for your time on our manuscript.