Author’s response to reviews

Title: Obesity, Cardiovascular Risk Factors, and Mortality among Older Thais: A Four-Year Follow-Up Study

Authors:

Patama Vapattanawong (prvp@mahidol.ac.th)
Wichai Aekplakorn (rawap@mahidol.ac.th)
Uthaithip Rakchanyaban (shurc@mahidol.ac.th)
Pramote Prasartkul (prpps@mahidol.ac.th)
Yawarat Porapakkham (yawaratp@yahoo.com)

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Author’s response to reviews: see over
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Dear Editor,

Re: Obesity, cardiovascular risk factors, and mortality among older Thais: A four-year follow-up study.

We are grateful for the reviewers’ valuable comments and suggestion. We have made considerable major changes in the main manuscript to address all concerns. We have revised the objectives of the study to be more focus on obesity and mortality and because of that the title of the manuscript has been changed to “Obesity and mortality among older Thai: a four-year follow-up study”.

We hope that we have addressed all the points.

Thank you for your consideration.

Best Regards,

Wichai Aekplakorn MD. PhD
Corresponding author

Response to reviewer comments

Reviewer 1

Discretionary Revisions
1. Is there any data on quality of life data from the NHES survey? If not, I would suggest adding this as a limitation.

There was no direct data on quality of life in the dataset, so we’re not able to look at it details, however, we’ve added about this point in the limitation.

2. The authors report using the education variable as socioeconomic status. However education only plays a partial role in determining socioeconomic status, which also includes income and occupation. Not having this data may be considered a limitation.

There are quite a number missing data in the income variables. So we decide not to use it.

Minor Essential Revisions
1. There are a number of grammatical errors within the text that should be corrected. There are also errors within the references i.e. Reference #22: Incorrect title.

The errors have been corrected.

2. Reference #30 is missing. The references are also not formatted properly.

The reference has been added.

3. Figure #1 is missing.
4. On page 4, the authors state, “From this linkage, older persons who died from all causes, except accidents and assault, and those without information on health risk or protective behaviors were excluded”, however I think they meant to say “included”.

It has been changed.

5. The authors use the BMI cutoffs of <18.5, 18.5-24.9, 25.0-29.9, and 30.0-34.9, which are the World Health Organization (WHO) recommended cutoffs for BMI, and should be referenced as such.

As the reviewer’s suggestion, it has been corrected.

6. On page 5, the authors describe the fruit and vegetable categories, stating 1 cup = 150 mL, however 1 cup is actually equal to 240 mL.

It has been corrected.

7. Please report the confidence intervals (+/- p values) in Table 3 instead of the standard errors.

95% Confidence interval are used instead of P-value.

8. In the footnotes below Table 3, “Model 2” is repeated twice.

Done.

9. Rounding of decimal places is not consistent in the tables.

Now, only one decimal has been used for percentage and 2 decimals for odds ratio.

10. There is no “Conclusion” heading.

Done.

11. Table 3 title is incomplete – the follow-up years are typed as 2004-200”.

Done.

12. I am unclear with the timelines for data collection - was the data collected between Jan 1st and Dec 31st of 2004? Please clarify.

The baseline data collection had been collected between Jan 15th and April 15th of 2004.

13. I would not consider the study to be a “4-year study” if the mean follow up time is 2.2 years.

The study ended at December 31th 2008. The 2.2 years is the mean of survival time of those who died. We have made this point clearer in the results by showing median survival time of the cohort.
Major Compulsory Revisions

1. I feel that the primary objective is a little unclear. The objective, “to examine the relationship of obesity and selected cardiovascular risk factors from the health survey with all-cause mortality among older persons”, is vague. Is obesity the primary variable of interest? Is there a lack of data specifically in the elderly Thai population? The authors refer to a gap in the literature where previous studies examined risk factors in the Thai population in mostly urban populations vs. rural populations as, however, this does not specifically relate to their objective. The statement of purpose, or the reason for conducting the study should be better defined. The authors should refer to previous research examining obesity and mortality in the elderly in the background information in obesity is their primary variable of interest.

As suggested, the objective was changed to “examine the relationship of body mass index with all-cause mortality. The introduction part has been rewritten to focus on BMI and mortality and the reason of doing the study has been elaborated in the introduction.

2. On page 5, the authors state “Besides risk factors of CVDs, two risk behaviors were of interest” fruit and vegetable consumption and physical activity”. This statement is unexpected – if those are variables “of interest”, they should be mentioned up front, at least as a secondary objective. My suggestion would be to focus on 1-3 variables of interest at most i.e. obesity and physical activity in older adults, instead of all possible risk factors.

As suggested, we decide to focus only on BMI and treat other variable as potential confounding factors.

3. The authors stratified their analyses by men and women but did not provide a reason for doing so. If they are specifically looking for gender differences in outcomes, then Table 1 should also be stratified by males and females.

Table 1 stratified by sex has been shown. The stratification was made because there are some degrees of differences in the magnitude of association by gender.

4. In the methods section, the authors report the total number analyzed, the response rate and missing data, however almost all of this information is then repeated in the results section. Having the totals in the results section alone is sufficient.

The information is retained only in the methods section.

5. It would be preferred to report median survival time vs. mean survival time or person-years follow up.
Done.

6. The number of people in each BMI category should be included in Table 1 and in the text. The authors refer to the “low number of people with BMI 30-34.9 and 35.0+” but only in the discussion, and only in percentages.

Done.

7. On page 8, the authors state, “In comparison with the reference category of each predictive variable, these hazard ratios among older women were obviously greater than among older men.” This statement is very confusing and I am unsure of what it is referring to, as some HRs were lower in women compared to men, and some were higher in women compared to men.

This sentence has been rewritten.

8. The authors refer to the BMI cutoffs that were chosen for their analysis as potentially inappropriate given that the WHO has more recently suggested using lower BMI cutoffs in Asian populations. Why were these not used then? Or could the authors have used both and determined if there were any differences in results?

As suggested, we reanalyzed that data using the BMI cut-off points for Asian population.

9. The authors have found a paradoxical finding between BMI and mortality – an inverse relationship which is opposite of the traditional risk factor epidemiology of BMI in the general population whereby as BMI increases, all cause mortality also increases. This has been termed the Obesity Paradox and has been observed consistently in the elderly population, however the authors make no mention of this in the introduction or the discussion. I think a discussion regarding the ‘obesity paradox’ in the elderly and how it ties in to your study should be included. The review by Oreopoulos et al, The Obesity Paradox in the Elderly: Potential Mechanisms and Clinical Implications Clinics in Geriatric Medicine, Volume 25, Issue 4, Pages 643-659 as well as a review by Artham et al “Obesity Paradox in the elderly: Is Fatter really Fitter?” (Aging Health, 2009 Vol 5: 177) and a review by Lavie et al “Obesity and Cardiovascular Disease Risk Factor, Paradox, and Impact of Weight Loss” (JACC 2009;53:1925) could be referred to.

The issue of obesity paradox has been included in the discussion part.

10. The authors mentioned that they had waist circumference and waist-to-hip ratio data. Although they chose to use BMI as the measure of obesity, there was no mention of why they chose BMI vs. the other two. It would be interesting to see if there are differences in mortality when different measures of obesity are used (or provide a reason for using BMI over the other anthropometric measures).

Thank you for the suggestion, this paper we decide to focus only on BMI, as we think that the measurement is more reliable.

11. In the discussion, there is no interpretation of the fruits and vegetable consumption findings or how they relate to previous studies examining this variable.
This issue was not highlighted in the results, as we treat it as a confounding factor.

12. There is no conclusion heading. I assume the last paragraph is the conclusion, however it is too vague and refers to “policy implications”, which was not mentioned previously in the paper.

Done. The conclusion has been rewritten.

13. The abstract conclusion is not supported by the data. The authors state that “this study supports evidence of increased mortality in low and high BMI”, but their adjusted analysis did not show increased mortality in the highest BMI groups.

The sentence has been rewritten.

14. The abstract results section is confusing. They refer to a J-shaped association between BMI and mortality, however this was seen in age-only adjusted analyses and not in the fully adjusted analyses. To truly determine if a “J-shaped” association exists, it would be helpful to perform fractional polynomial Cox Regression and then you could graph the results to display the mortality pattern.

The abstract has been rewritten.

We reanalyzed the data using to more detailed categories of BMI using cox hazard regression and plot the hazard ratio. By this method we think that it could provide a relatively good shape of the association. Frankly, we are not familiar with the fractional polynomial regression.

15. The authors use the Akaike’s Criteria Information to select the most parsimonious model for Cox Regression analysis. The rational for using this method is unclear. For one thing, the sample size is large enough that it would easily accommodate 14 variables (the full model). If the authors are specifically interested in the association between BMI and mortality and/or physical fitness and mortality, then they would want to adjust for all measured potential confounders vs. trying to choose the most parsimonious model – which would not present an advantage over entering all variables. I would suggest either entering all variables in to the model, or entering them as blocks where they group the similar variables together, i.e. first block age and sex, second block co-morbidities, third block physical activity etc. Also, it is more common to check for interaction between the main variable(s) of interest and age or gender, not between hypertension and diabetes as the authors have done, unless there is a specific clinical reason for doing so.

We reanalyzed the data using full model by including all independent variables that were significantly associated with outcome (at p-value<0.1) from the univariate analysis.

We’ve tested all the possible interactions between BMI and age, or BMI with gender or with hypertension or diabetes. There were no significant interaction between those pairs at P <0.2.

Reviewer 2
- Major Compulsory Revisions
The manuscript written by Vapattanawong et al, “Obesity, Cardiovascular Risk Factors, and Mortality among Older Thais: A Four-Year Follow-Up Study” is very interesting, but it is not original in Asian population as the author mentioned in his discussion (Gu D.et al 2006). Further, there are some issues and limitations regarding to the outcome, methods and results that need to be clarified and revised.

1. Abstract: The author should review the sentence, “a reverse J-like shape of association between BMI and all-cause mortality was observed”, which is not in agreement with the results presented in the table 3, and the following statement in the discussion section: “This Study was unable to confirm the reverse –J or U shape relationship between BMI and mortality as found in many studies”. The results summary should be clarified.

Its not totally clear from which models the hazard ratios were obtained as well as it seems that the author omitted the information about men ranging 30-34.9 kg/m2. As consequence the conclusion is not totally right since the author did not find a significant increased mortality among all BMI strata for both genders.

The results of associations were obtained from the final model. The abstract, results and discussion have been rewritten about this point.

1. Introduction: The author should add more discussion regarding the relationship between mortality and obesity among older people.

More sentences have been added to discuss about this point in the introduction.

2. Methods: The author never mentioned about past smokers as well as the prevalence of some comorbidities that are more frequent among older people, as cancer, chronic illness which are associated with lower BMI, even in a pre-clinical stage. Also, the author did not consider the waist circumference as a measure of obesity or tested different cut-offs previously described in Asian populations. Further, the author did not consider the additional multivariate adjustment by cigarette smoking, alcohol consumption, physical activity, education, beyond age, marital status, geographical area and education level as well as he did not perform separate analyses after excluding participants who were current or former smokers, heavy alcohol drinkers, or who had prevalent chronic illness at the baseline examination, or who died during the first 3 years of follow-up. In the statistical analyses the author mentioned about some results from the regressions models. This part should be moved to the results section. Finally, he forgot to mention about the statistical program.

We decide that we will focus on BMI variable, as the measurement is more reliable. We’ve reanalyzed the data and included ex-smoker as another dummy variable. The final model already included all the potential confounding variable (marital status, smoking, urban/rural, education, diabetes, hypertension, physical activity and fruit and veg consumption).

Additional analyses excluding those former, current smokers or heavy drinkers were made. Unfortunately, we don’t have data on chronic disease. The results of the analysis now are shown in table 3. Results of regression modeling have been moved to the results section. We used Stata version 10 software for the analysis.
3. Results: again, in this part the author mentioned about a reverse –J shaped pattern of mortality by BMI, which was found in both men and women (table 2). This issue needs to be rewritten since the author did not find significant results in higher BMI ranges regardless to gender. This affirmation is more controversial when the author also mentioned that “as a consequence of controlling for other variables, a reverse-J shape association between BMI and hazard was not retained.

The paragraph were rewritten.

- Minor Essential Revisions
  - In the table 1, its not make sense analyze the association between BMI as continuous variable with categorical variable.

The tables were rewritten.

- In the table 3, The author misled the model 4 for model 2 in the bottom line.

Done.

- Discretionary Revisions
  The author should consider analyzing the relationship of all-cause mortality with BMI ranges suggested for Asian people as well as with WC.

Additional cut-off points of BMI appropriated for the Asian people were used in the reanalysis.