PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of Obesity, Overweight and Underweight on Life Expectancy and Lifetime Medical Expenditures: The Ohsaki Cohort Study
AUTHORS	Masato Nagai, Shinichi Kuriyama, Masako Kakizaki, Kaori Ohmori-Matsuda, Toshimasa Sone, Atsushi Hozawa, Miyuki Kawado, Shuji Hashimoto and Ichiro Tsuji

VERSION 1 - REVIEW

REVIEWER	Ramon Luengo-Fernandez DPhil Health Economics Research Centre, University of Oxford, UK
REVIEW RETURNED	02/03/2012

THE STUDY	Some of the conclusions and highlights made by the authors both in the abstract and discussion are based on statistically non-significant findings. For example: in the abstract the authors report "In spite of their shorter life expectancy, obese participants required higher medical expenditure than normal weight participants". However, in their results, the authors report that for men there were no differences in life expectancy or medical expenditure (adjusted and non-adjusted) between normal and obese patients, and in women, differences were only identified for lifetime medical expenditure.
RESULTS & CONCLUSIONS	Some of the conclusions and highlights made by the authors both in the abstract and discussion are based on statistically non-significant findings. For example: in the abstract the authors report "In spite of their shorter life expectancy, obese participants required higher medical expenditure than normal weight participants". However, in their results, the authors report that for men there were no differences in life expectancy or medical expenditure (adjusted and non-adjusted) between normal and obese patients, and in women, differences were only identified for lifetime medical expenditure.
GENERAL COMMENTS	1) The results section and conclusions should be quantified. The finding that “In spite of their shorter life expectancy, obese participants required higher medical expenditure than normal weight participants” is based on statistically non-significant findings: for men there were no differences in life expectancy or medical expenditure (adjusted and non-adjusted) between normal and obese patients, and in women, significant differences were only identified for lifetime medical expenditure. Introduction: 2) Last sentence, paragraph 1, page 5. I do not really understand what the authors mean by “per month or per person”. Materials and methods: 3) Last sentence, paragraph 2, page 8. The last sentence is repetitive and virtually the same as the previous one. 4) First sentence, paragraph 1, page 10. What did the previous study evaluate? A brief sentence would be helpful.

	5) First sentence, paragraph 2, page 10. What is the index year? Year of death? Year of enrolment? 6) First sentence, paragraph 2, page 10. As it reads "... who died because of increasing medical expenditure before death", this sentence suggests that patients die as a direct result of increased medical expenditure. Please re-write. 7) Last sentence, page 11. Please provide reference to the purchasing power parity rate applied. Results: 8) Paragraph 1, page 12. In my opinion this paragraph would read better if there were no decimals to the medical expenditure. 9) Paragraph 1, page 12. How were unadjusted differences in medical expenditure between BMI categories evaluated? ANOVA? 10) Paragraph 4, page 14. The results from the multi-adjusted analysis on life-expectancy showed no statistically significant differences. At least p-values should be reported to make this clear. For medical expenditure, the differences were also non-statistically significant for men. P-values should, at a minimum, also be provided here. Discussion: 11) Paragraph 1, page 16. This paragraph should be quantified given that many of these differences are not statistically significant.

REVIEWER	Julien Dumurgier, MD, PhD, INSERM, Paris, France.
REVIEW RETURNED	02/03/2012

THE STUDY	This large meta-analysis of the relationship between BMI and mortality appears to be important and should be mentionned : Berrington de Gonzalez A et col. Body-Mass Index and Mortality among 1.46 Million White Adults. NEJM. 2010.
RESULTS & CONCLUSIONS	The authors conclude that obese participants have shorter life expectancy. However, this result is not strongly support by their analysis : mortality ratios and life exptectancy did not significantely differ among obese participants compared to normal weight, in multivariate analysis (p>0.05).

VERSION 1 – AUTHOR RESPONSE

COMMENTS OF THE REVIEWER AND AUTHORS' REPLIES
Journal: BMJ open
MS. Ref. No.: bmjopen-2012-000940
Title: Impact of Obesity, Overweight and Underweight on Life Expectancy and Lifetime Medical Expenditures: The Ohsaki Cohort Study

Comments from Dr. Ramon Luengo-Fernandez

1. Abstract:
The results section and conclusions should be quantified. The finding that "In spite of their shorter life expectancy, obese participants required higher medical expenditure than normal weight participants" is based on statistically non-significant findings: for men there were no differences in life expectancy or medical expenditure (adjusted and non-adjusted) between normal and obese patients, and in women, significant differences were only identified for lifetime medical expenditure.

[Authors' reply]
Thank you for your pertinent and important comments.
We mentioned "significantly" or "non-significantly".
And, we changed weaker conclusion.

[Changes in the revised manuscript]
[Page 3, Lines 16- Page 4, Lines 6]
In spite of their shorter life expectancy, obese participants might require higher medical expenditure than normal weight participants. In men aged 40 years, multiadjusted life expectancy for those who were obese participants was 41.4 years (95%CIs; 38.28-44.70), which was 1.7 years non-significantly shorter than that for normal weight participants (p=0.3184). Multiadjusted lifetime medical expenditure for obese participants was £112,858.9 (94,954.1-131,840.9), being 14.7% non-significantly higher than that for normal weight participants (p=0.1141). In women aged 40 years, multiadjusted life expectancy for those who were obese participants was 49.2 years (46.14-52.59), which was 3.1 years non-significantly shorter than for normal weight participants (p=0.0724), and multiadjusted lifetime medical expenditure was £137,765.9 (123,672.9-152,970.2), being 21.6% significantly higher (p=0.0005).

[Page 4, Lines 8- Page 4, Lines 10]
According to the point estimate, lifetime medical expenditure might appear to be higher for obese participants, despite their short life expectancy.

2. Introduction:
Last sentence, paragraph 1, page 5. I do not really understand what the authors mean by "per month or per person".

[Authors' reply]
Thank you for your pertinent and important comments.
Kuriyama et al. (reference 1) showed that underweight participants have higher mean medical expenditure per month. Meanwhile, Nakamura et al. (reference 4) showed that total medical expenditure per person is higher during 10 years follow-up.

3. Materials and methods:
Last sentence, paragraph 2, page 8. The last sentence is repetitive and virtually the same as the previous one.

[Authors' reply]
Thank you for your important comment and suggesting the better terms.
We deleted that sentence.

[Changes in the revised manuscript]
[Page 8, Lines 19-20]
Thus, the self-reported heights and weights were considered to be sufficiently valid.

4. Materials and methods:
First sentence, paragraph 1, page 10. What did the previous study evaluate? A brief sentence would be helpful.

[Authors' reply]
Thank you very much for your pertinent and important comments.

We mentioned about the previous subject of study.

[Changes in the revised manuscript]
[Page 10, Lines 2-3]
We conducted the same analysis as previous study about the association between walking, life expectancy, and lifetime medical expenditure.

5. Materials and methods:
First sentence, paragraph 2, page 10. What is the index year? Year of death? Year of enrolment?

[Authors' reply]
Thank you for suggesting the better terms.
We calculated medical expenditure from year of survived during follow-up period in survivors.

6. Materials and methods:
First sentence, paragraph 2, page 10. As it reads "... who died because of increasing medical expenditure before death", this sentence suggests that patients die as a direct result of increased medical expenditure. Please re-write.

[Authors' reply]
Thank you for your pertinent and important comments.
We re-wrote that sentence.

[Changes in the revised manuscript]
[Page 10, Lines 17-19]
We separately calculated medical expenditure for participants who survived through the index year and for those who died because previous study showed that medical expenditure increased before death.

7. Materials and methods:
Last sentence, page 11. Please provide reference to the purchasing power parity rate applied.

[Authors' reply]
Thank you for your important comment and suggesting the better terms.
We added the reference.

[Changes in the revised manuscript]
[Page 11, Lines 19]
We used a purchasing power parity rate of UK£ 1.00=JPN\ 140. 16

8. Results:
Paragraph 1, page 12. In my opinion this paragraph would read better if there were no decimals to the medical expenditure.

[Authors' reply]
Thank you very much for your pertinent and important comment.
We showed only integer number about the medical expenditure in that paragraph.

[Changes in the revised manuscript]
[Page 12, Lines 5-8]
The mean medical expenditure per year for survivors in men was £2,393 in underweight, £2,055 in normal weight, £2,231 in overweight, and £2,334 in obesity, respectively. In women, it was £2,375 in

underweight, £1,972 in normal weight, £2,317 in overweight, and £2,733 in obesity, respectively.

[Page 12, Lines 10-14]
Also, the mean medical expenditure in the year of death for participants in men was £15,445 in underweight, £16,973 in normal weight, £17,811 in overweight, and £17,878 in obesity, respectively. In women, it was £12,833 in underweight, £15,584 in normal weight, £17,059 in overweight, and £19,635 in obesity, respectively.

9. Results:
Paragraph 1, page 12. How were unadjusted differences in medical expenditure between BMI categories evaluated? ANOVA?

[Authors' reply]
Thank you for your pertinent and important comments.
We showed the mean medical expenditure per year calculated from ANOVA.
We mentioned about it.

[Changes in the revised manuscript]
[Page 12, Lines 8-10]
These differences of mean medical expenditure per year for survivors are statistically significant in men and women (ANOVA; $p<0.0001$).

10. Results:
Paragraph 4, page 14. The results from the multi-adjusted analysis on life-expectancy showed no statistically significant differences. At least p-values should be reported to make this clear. For medical expenditure, the differences were also non-statistically significant for men. P-values should, at a minimum, also be provided here.

[Authors' reply]
Thank you for your important comment and suggesting the better terms.
We showed p value and mentioned "significantly" or "non-significantly".

[Changes in the revised manuscript]
[Page 14, Lines 15- Page 15, Lines 1]
By multiadjusted analysis, obese men and women had approximately 1.7 years and 3.1 years non-significantly shorter life expectancy from the age of 40 years in comparison with men and women of normal weight, respectively (men; $p=0.3184$, women; $p=0.0724$). Meanwhile, obese men and women had approximately 14.7% non-significantly higher and 21.6% significantly higher lifetime medical expenditure in comparison with normal weight participants, respectively (men; $p=0.1141$, women; $p=0.0005$).

11. Discussion:
Paragraph 1, page 16. This paragraph should be quantified given that many of these differences are not statistically significant.

[Authors' reply]
Thank you for your pertinent and important comments.
We also showed p value and mentioned "significantly" or "non-significantly".

[Changes in the revised manuscript]
[Page 16, Lines 3-11]
The present results indicate that: 1) obese men and women have 14.7% non-significantly higher and

21.6% significantly higher multiadjusted lifetime medical expenditure than those of normal weight (men; p=0.1141, women; p=0.0005), even though their life expectancy is non-significantly shorter by 1.7 years and 3.1 years than those of normal weight participants, respectively (men; p=0.3184, women; p=0.0724); 2) underweight men and women have 5.2% and 3.4% non-significantly lower lifetime medical expenditure than those of normal weight (men; p=0.5174, women; p=0.3916) because men and women live 5.6 years and 5.3 years significantly less than those of normal weight, respectively (men; p<.0001, women; p<.0001).

Cments from Dr. Julien Dumurgier

1. This large meta-analysis of the relationship between BMI and mortality appears to be important and should be mentionned :
Berrington de Gonzalez A et col. Body-Mass Index and Mortality among 1.46 Million White Adults. NEJM. 2010.

[Authors' reply]
Thank you for your pertinent and important comments.
However, our study participants are Japanese. Thus instead of your suggested study, we mentioned about large pooled analyses of the association between BMI and mortality in Asia and Japan.
・Zheng et al. Association between body-mass index and risk of death in more than 1 million Asians. N Engl J Med 2011.
・Sasazuki et al. Body mass index and mortality from all causes and major causes in Japanese: results of a pooled analysis of 7 large-scale cohort studies. J Epidemiol 2011.

[Changes in the revised manuscript]
[Page 17, Lines 4-6]
Thus the association between BMI and life expectancy showed same trend with the pooled analyses of the association between BMI and all-cause mortality in Asia and Japan.

2. The authors conclude that obese participants have shorter life expectancy. However, this result is not strongly support by their analysis: mortality ratios and life exptectancy did not significantely differ among obese participants compared to normal weight, in multivariate analysis (p>0.05).

[Authors' reply]
Thank you for your pertinent and important comments.
As you suggested, we did not observe significant association. However, previous studies supported present results. In Japan, prevalence of obesity is only 3% (Yoshiike et al. Int J Obes Relat Metab Disord 1998). Thus the reason of non-significant association might be beta error because of lack of statistical power due to small number of obese participants.

[Changes in the revised manuscript]
[Page 19, Lines 20- Page 20, Lines 4]
Additionally, we did not observe significant association in obese participants without lifetime medical expenditure in women. However, our results are consistent with those of previous studies. In Japan, prevalence of obesity is only 3%. Thus the reason of non-significant association might be beta error because of lack of statistical power due to small number of obese participants.

[Page 20, Lines 7-8]
In summary, even though we observed non-significant association between obesity, life expectancy, and lifetime medical expenditure without lifetime medical expenditure in women, lifetime medical expenditure might appear to be higher for obese participants, despite their short life expectancy.

VERSION 2 – REVIEW

REVIEWER	Dr. Ramon Luengo-Fernandez Senior Researcher University of Oxford UK
REVIEW RETURNED	12/04/2012

GENERAL COMMENTS	The authors adequately addressed all my previous comments.