PEER REVIEW HISTORY

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Sarcopenia as a predictor of all-cause mortality among older nursing home residents: a systematic review and meta-analysis
AUTHORS	Zhang, Xiaoming; Wang, Conghua; Dou, Qingli; Zhang, Wenwu; Yang, Yunzhi; Xie, Xiaohua

VERSION 1 – REVIEW

REVIEWER	Tomohiko Kamo Department of Physical Therapy, School of Health Sciences, Japan University of Health Sciences, 2-555, Hirasuka, Satte-city, Saitama, 340-0145 Japan
REVIEW RETURNED	24-Jan-2018

GENERAL COMMENTS	The authors demonstrate clearly that sarcopenia is predictor of all-cause mortality among nursing home residents in meta-analysis. The manuscript is interesting, because sarcopenia is a frequent problem in nursing home residents. However, there are some major concerns about the overall clarity of the manuscript. Below are a few comments and recommendations for changes. Introduction Page 3 line 42: It is not right that prevalence of sarcopenia in nursing home. You should add more literature. In case you are interested, see below the references. Senior HE, Henwood TR, Beller EM, Mitchell GK, Keogh JW, Prevalence and risk factors of sarcopenia among adults living in nursing homes. Maturitas. 2015 Dec;82(4):418-23. Halil M et al, Sarcopenia assessment project in the nursing homes in Turkey. Eur J Clin Nutr. 2014 Jun;68(6):690-4. Page 4 line 9: Please add literature: "It has been shown that the mortality rate in nursing home is approximately eightfold higher than that in the community," Results Figure1: Please add number of studies to reasons for exclusion. How many studies have been excluded due to reviews, sample number <50 etc. . . .

	Table 1: Please add details of sarcopenia criteria. What methods was muscle mass measured (MRI, CT, DXA, BIA ,CC…?)? How many points was cut-off of muscle mass? The scientific literature concentrating on sarcopenia in nursing home residents is scarce. Therefore, muscle mass measurements are not unified. Similarly, please add criteria of physical performance and muscle strength. Please add results of subgroup analysis according to different diagnosis tools for muscle mass. Please add risk of bias summary using Newcastle Ottawa scale: review author's judgements about each risk of bias item for each included study. Figure 4: There is only one study of less 100 samples. Therefore, you should modify or delete subgroup analysis of the meta-analysis according to sample size. You should add results of another subgroup analysis.

REVIEWER	Laura Schaap Vrije Universiteit Amsterdam, the Netherlands Sarcopenia
REVIEW RETURNED	24-Jan-2018

GENERAL COMMENTS	This review describes a systematic review and meta analyses of studies on sarcopenia and mortality among nursing home residents. My main issue is the poor English and scientific writing in this paper, which makes it very hard to read. Other concerns: Why did the authors not include studies with a study sample smaller than 50 persons? How many studies were excluded based on this criterion? Studies among nursing home residents often have a small sample size because of this setting, but can still provide important information of the review. Furthermore, subgroup analyses are performed based on sample size. However, the subgroup with a sample size <100 only includes 1 study, which is not the same as a subgroup. Regarding the in- and exclusion criteria: what is meant by "insufficient date"? The description of the EWGSOP definition of sarcopenia is not clear. Table 1: some columns are redundant, for example sarcopenia criteria and adjusted or crude HR/OR. Instead of describing whether the results are unadjusted or adjusted, include all confounders that are included in the studies. The discussion paragraph could be improved. Describe differences across the included studies and how this may effected the results of the study: differences in confounders used in the individual studies, mean age etc. Could the authors elaborate on the mechanisms behind the observed association? I would include some discussion about low muscle mass, which is highly associated with mortality, especially in the most vulnerable older persons. A low muscle mass is part of the EWGSOP definition, but other definitions also exist. Please elaborate on this as well.

REVIEWER	Irene SL Zeng University of Auckland, New Zealand.
REVIEW RETURNED	05-Apr-2018

GENERAL COMMENTS	The systematic review and meta-analysis study includes six eligible studies to investigate if sarcopenia is a risk factor of mortality in elderly nursing home residents. It has included a large number of studies in the screening phase. I summarize my review comments as follows: Strength: 1) It is the first systematic review and meta-analysis on this topic for elderly nursing home residents. 2) The Analysis were conducted by two reviewers independently. Improvements: 1) Study selection: a very large number of studies were pre-screened (based on the flow chart, 1965 studies were reduced to 85), how were the final six studies selected with guarantee that no other eligible studies were missed. 2) Analytical method: Odds ratio (OR) and Risk ratio (RR) should not be included in the pooled analysis with hazard ratio. 3) Analytical method: Are the adjusted HR are derived from models with different explanatory variables? If they were from different models, then the pooled summary should use the unadjusted HR which only have one explanatory variable (sarcopenia). 4) Analytical method: Some subgroup analysis should not be conducted due to a small number of studies. 5) PRISMA check list method 7: Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. No information of dates of coverage is listed in the paper. Minor comments: 1) Spaces are required between words in many sentences. 2) Abstract and article need more editing efforts. A reference paper on the similar topic to be considered: Jones K, Gordon-weeks A, Coleman Claire. Radiologically Determined Sarcopenia Predicts Morbidity and Mortality Following Abdominal Surgery: A Systematic Review and Meta-Analysis. World Journal of Surgery. September 2017, Volume 41, Issue 9, pp 2266–2279

VERSION 1 – AUTHOR RESPONSE

Replies to Reviewer 1

1. Page 3 line 42: It is not right that prevalence of sarcopenia in nursing home. You should add more literature. In case you are interested, see below the references.
Senior HE, Henwood TR, Beller EM, Mitchell GK, Keogh JW, Prevalence and risk factors of sarcopenia among adults living in nursing homes. Maturitas. 2015 Dec;82(4):418-23.
Halil M et al, Sarcopenia assessment project in the nursing homes in Turkey. Eur J Clin Nutr. 2014 Jun;68(6):690-4.

Response: Thank you very much for your question. The prevalence of sarcopenia in nursing homes is rather higher and the rates rise up to 85.4%[6],and 14–33% among Dutch and Italian adults residing in nursing homes[7].Correction has been made in the revised manuscript.

2. Page 4 line 9: Please add literature: “It has been shown that the mortality rate in nursing home is approximately eightfold higher than that in the community

Response: Thank you very much for your question. We have to admitted that it is our mistake. Previous study showed that 20% to 24% of the death occurs in nursing homes. Whereas, the mortality rate of the elderly in the community is 8.9-12.4%. Therefore, the mortality rate in nursing home is approximately twofold higher than that in the community.

3. Figure1: Please add number of studies to reasons for exclusion. How many studies have been excluded due to reviews, sample number <50 etc. . . .

Response: Thanks for raising this critical issue. Of these articles, thirty were removed duo to not cohort studies(e.g., review articles, conference documents, Cross-sectional study, Case-Control Study) and six was removed because of having no clear definition of Sarcopenia, moreover, forty-one removed duo to different study population: community- dwelling, Patients in hospital, and used the same cohorts (n = 2). These studies were screened according to the predefined inclusion and exclusion criteria for including in the meta-analysis, resulting in a total of six eligible studies (Figure.1).

4. Table 1: Please add details of sarcopenia criteria. What methods was muscle mass measured (MRI, CT, DXA, BIA ,CC…?)?

Response: Thank you very much for your question. We have added the detailed information in the table 2.

5. How many points was cut-off of muscle mass?

Response: Thank you very much for your question. The cut-off points are the major difference in these definitions, because of different tool of muscle mass, we have provided detailed information in table 2.

6. The scientific literature concentrating on sarcopenia in nursing home residents is scarce. Therefore, muscle mass measurements are not unified. Similarly, please add criteria of physical performance and muscle strength.

Response: Thank you very much for your question, we have added table 2 that contains all the detailed information.

7. Please add results of subgroup analysis according to different diagnosis tools for muscle mass.

Response: Thanks for your thoughtful suggestion. Our study showed that sarcopenia was significantly associated with the risk of morbidity among nursing home residents when using BIA to diagnose muscle mass (pooled effect size=1.88,95% CI =1.39- 2.53, p=0.00), whereas it was not associated when using anthropometric measures to diagnosis muscle mass (pooled effect size=1.79,95% CI=0.89-3.59, p=0.10).

8. Please add risk of bias summary using Newcastle Ottawa scale: review author's judgements about each risk of bias item for each included study.

Response: Thanks for your thoughtful suggestion. We have added detailed information in our revised manuscript in table 3.

9. Figure 4: There is only one study of less 100 samples. Therefore, you should modify or delete subgroup analysis of the meta-analysis according to sample size. You should add results of another subgroup analysis.

Response: Thank you for your insightful suggestion. We have deleted the subgroup analysis of sample size because only one study is less 100 samples and added the subgroup of different diagnosis tools.

Replies to Reviewer 2

1. My main issue is the poor English and scientific writing in this paper, which makes it very hard to read.

Response: Thank you very much for your insightful suggestion. Firstly, we are sorry for the poor readability of our previous article. Our revised manuscript has been edited and proofread by a professional copyediting agency called webshop Elsevier.We hope the revised version will be more readable.

2. Why did the authors not include studies with a study sample smaller than 50 persons?

Thank you very much. we are sorry to make this mistake, and we have corrected it.

3. How many studies were excluded based on this criterion? Studies among nursing home residents often have a small sample size because of this setting, but can still provide important information of the review.

Thanks for your insightful question. we agree with your idea. Studies among nursing home residents with small sample can still provide important information. Therefore, our team re-examined all of our previous literatures. However, we didn't find articles with less than 50 sample size could meet our criteria. Most important, the item with less 50 sample size in our exclusion criteria should delete in case of causing a misunderstand for the readers.

4. Furthermore, subgroup analyses are performed based on sample size. However, the subgroup with a sample size <100 only includes 1 study, which is not the same as a subgroup.

Thanks for your thoughtful suggestion. We have deleted the subgroup of sample size and added the subgroup of different diagnosis tools.

5.Regarding the in- and exclusion criteria: what is meant by "insufficient date"?

Thank you for your question. We are really sorry to make this mistake. Actually, the word of "date" should be corrected as "data".

6. The description of the EWGSOP definition of sarcopenia is not clear.

Thank you for your thoughtful question. According to the EWGSOP recommendation, diagnosis of sarcopenia required the documentation of low muscle mass plus the documentation of either low muscle strength or low physical performance.

7. Table 1: some columns are redundant, for example sarcopenia criteria and adjusted or crude HR/OR. Instead of describing whether the results are unadjusted or adjusted, include all confounders that are included in the studies.

Thank you for your question. Correction has been made in the revised manuscript showed in table1.

8. The discussion paragraph could be improved. Describe differences across the included studies and how this may effected the results of the study: differences in confounders used in the individual studies, mean age etc.

Thank you very much. Correction have been displayed in our revised manuscript.

9. Could the authors elaborate on the mechanisms behind the observed association? I would include some discussion about low muscle mass, which is highly associated with mortality, especially in the most vulnerable older persons.

Thank you for your insightful suggestion. The association between sarcopenia and mortality may be explained by the hypothesized adverse effects of a low muscle mass in older persons. Studies showed that low muscle mass is highly associated with increased mortality8, 9. In addition, elderly people in nursing homes are at high risk of malnutrition10, which aggravates low muscle mass, resulting in an increased mortality rate. For more information about the mechanisms behind the observed association has been showed in the discussion part of our revised manuscript.

10.A low muscle mass is part of the EWGSOP definition, but other definitions also exist. Please elaborate on this as well.

Thank you very much for your question. The EWGSOP recommends using the presence of both low muscle function (strength or performance) and low muscle mass for the diagnosis of sarcopenia. Thus, diagnosis of sarcopenia in the present study required the documentation of low muscle mass plus the documentation of either low muscle strength or low physical performance.

Replies to Reviewer 3
1. Study selection: a very large number of studies were pre-screened (based on the flow chart, 1965 studies were reduced to 85), how were the final six studies selected with guarantee that no other eligible studies were missed.

Thank you very much for your question. Actually, Screening was performed independently by two blinded reviewers (Xiaoming Zhang and Wenwu Zhang). In cases of disagreement on inclusion or exclusion of studies, this issue was discussed until consensus was reached by the reviewers, otherwise, the arbitration (yunzhi Yang) would make a decision.

2. Analytical method: Odds ratio (OR) and Risk ratio (RR) should not be included in the pooled analysis with hazard ratio.

Thank you very much for your insightful question and advice. We agree that Odds ratio (OR) and Risk ratio (RR) is not equivalent to HR in principle. Whereas, RR was considered equivalent to HR in our prospective cohort studies, which was reported in Carole Willi's study[11] and Ahmed N Mahmoud's study[12]. If a study reported the effect size as an OR, it will be converted to RR by using a previously described formula[7]. Therefore, instead of excluding the article reported OR or RR to make pooled analysis, we believe that the conversion would make the pooled effect size more reasonable. We hope professor Irene SL Zeng could accept our advice.

3. Analytical method: Are the adjusted HR are derived from models with different explanatory variables? If they were from different models, then the pooled summary should use the unadjusted HR which only have one explanatory variable (sarcopenia).

Thank you very much for your thoughtful suggestion. The adjusted HR was from different models. In fact, we believe that using adjusted HR for pooled analysis will be more reliably, because it can

maximally reduce confounding bias. When we performed the pooled analysis with unadjusted HR, Sarcopenia was significantly associated with a higher risk for all-cause mortality among nursing home residents (pooled HR=2.31, 95% confidence interval [95% CI] =1.53-3.49, I2 =46.3%,p=0.097), which was showed in Figure "unadjusted HR pooled analysis". Although the result was consistent with the previous, the Heterogeneity was increased and the 95% confidence interval was also widened so that the result was overestimated when used unadjusted HR to perform the pooled analysis.

4. Analytical method: Some subgroup analysis should not be conducted due to a small number of studies.

Thank you very much. We have deleted the subgroup analysis of sample size and added the subgroup of different diagnosis tools.

5. PRISMA check list method 7: Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. No information of dates of coverage is listed in the paper.

Thank you very much for your question. Correction have been displayed in our revised manuscript.

6. Spaces are required between words in many sentences.

Thank you very much for your question. Correction has been made in our revised manuscript.

7. Abstract and article need more editing efforts.

Thank you very much for your question. The abstract and article have been improved in our revised manuscript.

8. A reference paper on the similar topic to be considered:
Jones K, Gordon-weeks A, Coleman Claire. Radiologically Determined Sarcopenia Predicts Morbidity and Mortality Following Abdominal Surgery: A Systematic Review and Meta-Analysis. World Journal of Surgery. September 2017, Volume 41, Issue 9, pp 2266–2279.

Thank you very much for your question. After reading this article carefully, it is clear that this article has helped us a lot. Sincerely, we thank you for your advice.

9. FORMATTING AMENDMENTS (if any)

Thank you very much for your question. Amendments have been displayed in our revised manuscript.

10. Required amendments will be listed here; please include these changes in your revised version:

Thank you very much for your question, all amendments have been included in our revised version.

1. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the european working group on sarcopenia in older people. Age Ageing. 2010;39:412-423
2. Soriano CA, Sarmiento WD, Songco FJ, Macindo JR, Conde AR. Socio-demographics, spirituality, and quality of life among community-dwelling and institutionalized older adults: A structural equation model. Archives of gerontology and geriatrics. 2016;66:176-182

3. de Oliveira SC, dos Santos AA, Pavarini SC. [the relationship between depressive symptoms and family functioning in institutionalized elderly]. Revista da Escola de Enfermagem da U S P. 2014;48:66-72
4. Scocco P, Rapattoni M, Fantoni G. Nursing home institutionalization: A source of eustress or distress for the elderly? International journal of geriatric psychiatry. 2006;21:281-287
5. Mitchell JM, Kemp BJ. Quality of life in assisted living homes: A multidimensional analysis. The journals of gerontology. Series B, Psychological sciences and social sciences. 2000;55:P117-127
6. Bahat G, Saka B, Tufan F, Akin S, Sivrikaya S, Yucel N, et al. Prevalence of sarcopenia and its association with functional and nutritional status among male residents in a nursing home in turkey. The aging male : the official journal of the International Society for the Study of the Aging Male. 2010;13:211-214
7. Grant RL. Converting an odds ratio to a range of plausible relative risks for better communication of research findings. BMJ (Clinical research ed.). 2014;348:f7450
8. Brown JC, Harhay MO, Harhay MN. Appendicular lean mass and mortality among prefrail and frail older adults. The journal of nutrition, health & aging. 2017;21:342-345
9. Cesari M, Pahor M, Lauretani F, Zamboni V, Bandinelli S, Bernabei R, et al. Skeletal muscle and mortality results from the inchianti study. The journals of gerontology. Series A, Biological sciences and medical sciences. 2009;64:377-384
10. Vandewoude MF, Alish CJ, Sauer AC, Hegazi RA. Malnutrition-sarcopenia syndrome: Is this the future of nutrition screening and assessment for older adults? J Aging Res. 2012;2012:651570
11. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: A systematic review and meta-analysis. Jama. 2007;298:2654-2664
12. Mahmoud AN, Mentias A, Elgendy AY, Qazi A, Barakat AF. Migraine and the risk of cardiovascular and cerebrovascular events: A meta-analysis of 16 cohort studies including 1 152 407 subjects. 2018;8:e020498

VERSION 2 – REVIEW

REVIEWER	Tomohiko Kamo Japan University of Health Sciences, Japan
REVIEW RETURNED	30-May-2018

GENERAL COMMENTS	Thank you for this carefully revised version. To my opinion the paper can be accepted by the journal.

REVIEWER	Laura Schaap VU University Amsterdam, the Netherlands
REVIEW RETURNED	29-May-2018

GENERAL COMMENTS	The manuscript's readability has increased significantly. There are a few issues I would like to see resolved before publication. In de box Strengths and limitations of this study: point 4. The studies included in this study were insufficient: what is meant by the authors? Is the number of studies insufficient? One of the exclusion criteria involves "no clear definition of sarcopenia" . When is a definition considered not clear? Eventually, only studies that uses the EWGSOP definition were included in the study. Did the authors use this definition to in- or exclude papers? If so, please explain this in the methods. In the discussion this issue ("We adopted the same diagnostic criteria for sarcopenia (EWGSOP) and the same type of population") suggests that it was an inclusion criterium.

	Furthermore, in the discussion it is mentioned that there is a difference in association when length of follow-up is considered. However, the HR for both short and long term follow-up is the same, HR=1.87. The power for the short term analyses was to small to have a significant result. Therefore, I don't think that there actually is a difference that needs to be explained. The sentence " The underlying mechanisms between sarcopenia and a higher risk of all-cause mortality did not have a conclusion" is unclear. Please rephrase. I don't consider the fact that you have small heterogeneity a strength of this study. It is only an effect of your research question. Also the fact that studies included different confounders is not a limitation of your study (only of the studies that you included). I suggest to delete these from the discussion. There are several errors in table 1 (EWGSOP). The columns Sarcopenia criteria and Outcome is redundant. I would also include the actual confounders that are used in the studies. Table 2: How is it possible that some studies have no cut-off points for handgrip strength or gait speed? How can a definition be used without a cut-off?

REVIEWER	Irene SL Zeng University of Auckland
REVIEW RETURNED	05-Jun-2018

GENERAL COMMENTS	Congratulations to all of the authors for making such good efforts in the revised version. It has addressed some of the previous comments. In the analytical method, there remains several issues listed as follows: 1) Analytical method: Please give more explanations of using The HR to approximate RR in the statistical method. Similar like the quoted paper in the method section. 2) Please add sensitivity analysis which exclude those studies reporting RR and OR, and compare the result with including these studies. 3) The analysis shall use the ln(RR) which is the general approach for ratio in meta-analysis, because the RR or (HR) is not normally distributed. 4) In the method section, where it states “If heterogeneity was found to be reasonably high between studies, the random-effects model was used”. Please specify which model used the random-effect models and which one use the fixed –effect models. Result presentation: Abstract: p value please present as its real number ; if it is <0.001, then use <0.001 instead of 0.00. Table 1: please include the mortality rate for each study. Discussion: Acknowledge the limitation includes, 1. Using approximation of OR to RR, and from RR to HR. 2. Ignoring the different adjusted confounding factors of the derived HR from different studies.

	Minor comments: Page 53: “not cohort study”, should it be non-cohort study?

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Tomohiko Kamo

Response: Sincerely, thank you very much for your help and advice.

Reviewer: 2
Reviewer Name: Laura Schaap

1. In de box Strengths and limitations of this study: point 4. The studies included in this study were insufficient: what is meant by the authors? Is the number of studies insufficient?

Response：Thank you very much for your question. We have to admit that some subgroup analysis, for example, subgroup of diagnostic criteria, subgroup of sex, can’t be performed in our study because of the insufficient number of studies. We have rephrased the sentence to make it more clearly.

2. One of the exclusion criteria involves "no clear definition of sarcopenia". When is a definition considered not clear?

Response: Thank you very much for your question. When the study only use components or subdomains of sarcopenia criteria (e.g., muscle mass, muscle strength) to explore the association with mortality, we consider the studies can’t provide clear definition of sarcopenia.

3. Eventually, only studies that uses the EWGSOP definition were included in the study. Did the authors use this definition to in- or exclude papers? If so, please explain this in the methods. In the discussion this issue ("We adopted the same diagnostic criteria for sarcopenia (EWGSOP) and the same type of population") suggests that it was an inclusion criterium.

Response: Thank you very much for your question. EWGSOP definition is not used to in- or exclude papers in our study, we are so sorry to make this mistake here. In fact, our study contains two definitions of sarcopenia, the European Working Group on Sarcopenia in Older People (EWFSOP) proposed by Cruz-Jentoft, which was used in five studies. Whereas, in the study of Kimyagarov S, it used NIH-sponsored workshop[1] that refers specifically to involuntary loss of skeletal muscle mass and consequently of strength as sarcopenia. Correction has been made in our revised manuscript.

4. Furthermore, in the discussion it is mentioned that there is a difference in association when length of follow-up is considered. However, the HR for both short and long term follow-up is the same, HR=1.87. The power for the short term analyses was too small to have a significant result. Therefore, I don't think that there actually is a difference that needs to be explained.

Response: Thank you for your insightful suggestion. We agree with your viewpoint， Because there are only two studies containing short term subgroup analysis, so the power for short term analyses was actually not strong. Therefore, more perspective cohort studies about this issue must be conducted in the future.

5. The sentence " The underlying mechanisms between sarcopenia and a higher risk of all-cause mortality did not have a conclusion" is unclear. Please rephrase.

Response: Thank you very much for your question, the underlying mechanisms between sarcopenia and a higher risk of all-cause mortality were unable to draw conclusion.

6. I don't consider the fact that you have small heterogeneity a strength of this study. It is only an effect of your research question. Also the fact that studies included different confounders is not a limitation of your study (only of the studies that you included). I suggest to delete these from the discussion.

Response: Thank you for your insightful suggestion. We'd like to accept your good suggestion in our revised manuscript. Correction has been made in our revised manuscript.

7. There are several errors in table 1 (EWGSOP). The columns Sarcopenia criteria and Outcome is redundant. I would also include the actual confounders that are used in the studies.

Response: Thank you for your insightful suggestion. Correction has been made in our revised manuscript.

8. Table 2: How is it possible that some studies have no cut-off points for handgrip strength or gait speed? How can a definition be used without a cut-off?

Response: Thank you for your insightful question. we are sorry to made this mistake here. Our study contains two definitions of sarcopenia, the European Working Group on Sarcopenia in Older People (EWFSOP)[2] proposed by Cruz-Jentoft, which was used in five studies. Whereas, in the study of Kimyagarov S, it used NIH-sponsored workshop[1] that refers specifically to involuntary loss of skeletal muscle mass and consequently of strength as sarcopenia. Therefore, there is no cut-off point for gait speed. Correction has been made in our revised manuscript.

Reviewer: 3
Reviewer Name: Irene SL Zeng

1. Analytical method: Please give more explanations of using
The HR to approximate RR in the statistical method. Similar like the quoted paper in the method section.

Response: Thank you for your insightful suggestion. Because all included studies are prospective cohort studies, the HR or RR is the effect of the cohort study. HR or RR means that the risk of mortality in the older people with sarcopenia is increased/decreased, when compared with older people without sarcopenia. If the RR or HR is equal to 0.89 (0.77-0.91), it shows that participant with Sarcopenia are associated with a 11% decrease risk of all-cause mortality, compared with those without sarcopenia. Conversely, RR or HR was equal to 1.89 (1.77-1.91). Participant with Sarcopenia are associated with 89% increase risk of all-cause mortality, compared with those without sarcopenia. Therefore, we think the HR approximates RR in the statistical method.

2. Please add sensitivity analysis which exclude those studies reporting RR and OR, and compare the result with including these studies.

Response: Thank you very much for your question. We conducted a sensitivity analysis of sarcopenia and falls by omitting one study each time and pooling the others to find which study influenced the main effect. No statistically significant changes were found, as shown in Figure 6.

3. The analysis shall use the ln(RR) which is the general approach for ratio in meta-analysis, because the RR or (HR) is not normally distributed.

Response: Thank you for your insightful suggestion. We totally agree with your opinion. Actually, we use ln(RR) or ln(HR) for meta-analysis. Correction has been made in our revised manuscript.

4. In the method section, where it states "If heterogeneity was found to be reasonably high between studies, the random-effects model was used". Please specify which model used the random-effect models and which one use the fixed –effect models.

Response: Thank you very much for your question. all the models were used fixed-effect model. we have displayed the fixed-effect model in all of the figures.

5. Abstract: p value please present as its real number; if it is <0.001, then use <0.001 instead of 0.00.

Response: Thank you very much for your question. p value for the result was 0.000 when use STATA version 14.0 to perform Statistical analysis. We use the real number of p value.

6. Table 1: please include the mortality rate for each study.

Response. Thank you very much for your question. We have provided mortality rate for each study in Table1.

7. Acknowledge the limitation includes,
(1). Using approximation of OR to RR, and from RR to HR.
(2). Ignoring the different adjusted confounding factors of the derived HR from different studies.

Response: Thank you very much for your question. We have added these two limitations in the discussion.

8. Page 53: "not cohort study", should it be non-cohort study?

Response : thank you very much, we have change the word" not cohort study'' to non-cohort study.

1. Roubenoff R. The pathophysiology of wasting in the elderly. The Journal of nutrition 1999;129(1S Suppl):256s-59s doi: 10.1093/jn/129.1.256S[published Online First: Epub Date]|.
2. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age and ageing 2010;39(4):412-23 doi: 10.1093/ageing/afq034[published Online First: Epub Date]|.

VERSION 3 – REVIEW

REVIEWER	Irene SL Zeng University of Auckland New Zealand
REVIEW RETURNED	20-Jul-2018

GENERAL COMMENTS	Thank you for the revision. There are only several places requiring clarity and further edits. Please find them as follows: Abstract Line 29-36: This sentence is not clearer to me. If authors mean to

	state that the length of follow-up is associated with mortality, then meta-regression should be used. I think authors mean to say, Sarcopenia was significantly associated with all-cause mortality in studies with a follow-up period of 1 year or more, but not found to be significant in studies with a follow-up less than 1 year. Please provide number of patients in each subgroup analysis in the text, the non-significant results in studies with follow-up period less than 1 year could be caused by smaller number of patients (only 2 studies) in this subgroup. Please add comments for this result in discussion. Analysis method and result: Please provide reference to support that length of follow up and BIA are known factors that are associated with mortality. This will justify the reason for a subgroup analysis based on length of follow up and BIA. Results presentation: All p value =0.000 please change to p<0.0001. Please check typo and sentences in lines: 1. Page 6: Line 36-40. 2. Page 7: Line 38-40. Starts from “Follow-up periods were not…”. 3. Page 8: subgroup analysis results needs more edit , starts from “Two studies with a follow-up period” 4. Page 8: line47. “Each time and pooing “ 5. Page 9: discussion. The I2 is shown to be 0% by rounding, please provide the exact one and change the perfect to a small. Figure 4: there is omitted text in the label.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 3

Reviewer Name: Irene SL Zeng

1. Abstract

Line 29-36: This sentence is not clearer to me. If authors mean to state that the length of follow-up is associated with mortality, then meta-regression should be used. I think authors mean to say, Sarcopenia was significantly associated with all-cause mortality in studies with a follow-up period of 1 year or more, but not found to be significant in studies with a follow-up less than 1 year.

Author response: Thank you very much. Actually, we totally agreed with your opinion and we have rephrased the sentence. In addition, the subgroup analysis demonstrated that sarcopenia was associated with all-cause mortality (pooled HR 1.87, [95%CI] =1.38- 2.52, p<0.001) when studies with a follow-up period of 1 year or more were analysed; however, this was not found for studies with the follow-up period less than 1 year.

2. Please provide number of patients in each subgroup analysis in the text, the non-significant results in studies with follow-up period less than 1 year could be caused by smaller number of patients (only 2 studies) in this subgroup. Please add comments for this result in discussion.

Author response: we have provided numbers of patients in each subgroup analysis in the text, and added comments for this result in discussion. It is noticed that there were only 231 cases in the two studies with the follow-up period of less than 1 year and it is likely that the number of studies and included cases for the short term analysis were too small to have a significant result. Therefore, more perspective cohort studies about this issue must be conducted in the future.

3. Analysis method and result:

Please provide reference to support that length of follow up and BIA are known factors that are associated with mortality. This will justify the reason for a subgroup analysis based on length of follow up and BIA.

Author response: Thank you very much. We have added reference to support that the length of follow up and BIA are known factors that are associated with mortality

4. Results presentation:

All p value =0.000 please change to p<0.001. Please check typo and sentences in lines:

Author response: Thank you very much, we have change p value =0.000 to p<0.001 in our manuscript.

1. Page 6: Line 36-40.

2. Page 7: Line 38-40. Starts from “Follow-up periods were not…”.

3. Page 8: subgroup analysis results needs more edit , starts from “Two studies with a follow-up period”

4. Page 8: line47. “Each time and pooing “

Author response: Thank you very much. The correction has been made in the revised manuscript.

5. Page 9: discussion. The I2 is shown to be 0% by rounding, please provide the exact one and change the perfect to a small.

Author response: Thank you very much. Because the result of data made by STATA version 14.0 were actually showed the original result in the figure, we have change the word “perfect “ to a small, the correction has been made in the revised manuscript.

6 Figure 4: there is omitted text in the label.

Author response: Thank you very much. The correction has been made in the revised manuscript.

VERSION 4 – REVIEW

REVIEWER	Irene SL Zeng University of Auckland, New Zealand
REVIEW RETURNED	19-Aug-2018

GENERAL COMMENTS	Minor edit: Figure 4 label needs to change. Page 8 line 49 has one typo.