PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Prevalence and Temporal Trends of Pre-sarcopenia Metrics and Related Body Composition Measurements from the 1999-2006 NHANES survey
AUTHORS	Li, Ji-Bin; Wu, Yuwan; Gu, Dantong; Li, Huajun; Zhang, Xi

VERSION 1 – REVIEW

REVIEWER	Leo Westbury MRC Lifecourse Epidemiology Unit University of Southampton UK
REVIEW RETURNED	15-Dec-2019

GENERAL COMMENTS	In the abstract, I would recommend the following: define 'NHANES'; change the phrases 'youth-orientated tendency' and 'reverse tendency' as they are a little unclear; and mention the statistics for non-Hispanic white participants in the results as they are mentioned in the conclusion. It states that the prevalence of sarcopenia among adults aged 55 years and older is high (page 4, line 15). It would be helpful for the reader if this prevalence was stated. It states that loss of muscle can lead to a higher metabolic rate which can result in fat gain (page 4, lines 24-29). Shouldn't this read as 'lower metabolic rate'? I feel that the introduction could explain the condition of sarcopenic obesity which can have more serious health implications than either of these two conditions in isolation. The introduction could also outline that there are a variety of sarcopenia definitions but no consensus definition. In the section 'Study design and participants', the number of participants included in the NHANES III cohort and in the analytical sample could be stated. Only low appendicular skeletal muscle mass is used to define sarcopenia (page 5, line 58). However, the cited paper (reference 30) recommends the presence of low muscle mass and low muscle function (strength or physical performance) to define sarcopenia. Please justify why you are describing this condition as sarcopenia when it is really just a measure of muscle mass adjusted for height. Please explain how the variables for heart rate, VO2 max and CVD fitness were ascertained and defined.

	It states that in 1999-2000 (n=9), 49.6% were women. What does 'n=9' mean in this context? Some non-significant trends are described as increases and some are described as remaining stable (Page 9, lines 5-28). It would be helpful for the reader if these were described consistently. It states that participants who had high education levels were more likely to have a lower prevalence of sarcopenia compared to the lowest category of education (page 9, lines 35-40). However, I don't think this was the case in 1999-2000. It states that obesity prevalence significantly increased from 21.9% to 24.0% in the 18-39 group but then a non-significant p-value is stated (page 11, line 24). Please clarify. It states 'P for trend=0.229' among women and then '(all P-values for trend<0.001)' (page 11, line 19). These two statements seem to contradict each other. It states that similar trends of obesity prevalence were observed in non-Hispanic whites and Mexican Americans (Page 11, lines 28–33). Please clarify as the first group shows a significant increasing trend and the latter shows no significant trend. It states there was a large reduction in ASM and SMI (Page 11, lines 35–38). I don't think this supports the results in Table 3 or Figure 2A. It states that there were not significant sex differences over time in relation to sarcopenia prevalence (page 13, line 58). However, Table 2 shows significant sex differences in 2005-2006. In the discussion, there is a statement that sarcopenia prevalence decreased in men but not in women and several possible reasons for this are offered (page 14, lines 3-50). This seems to contradict the results in Table 2 showing that trends over time were not significant among men or women. The prevalence of sarcopenia among non-Hispanic blacks is stated as around 1% in 1999-2000, 7% in 2001-4 and then 26% in 2005-6. Such huge increases over such short durations do not seem plausible. Have you investigated reasons for this such as considerably more very old (>80 years) non-hispanic blacks being included in the sample at later years? I feel that grouping all participants 60 years of age and older into one group may mask the potentially large difference in prevalence and trends of sarcopenia between those in their early 60s and those in their late 80s. Are the patterns similar if more age bands are used within this age range? Regarding the figures, please define abbreviations and correct '1988' in the Figure 1 Legend. The footnotes in Table 2 state that sarcopenia was defined according to the DIA criteria. What does 'DIA' stand for?

REVIEWER	ALEMAN-MATEO H Research Center for Food and Development, Hermosillo, Sonora, Mexico.

REVIEW RETURNED	07-Feb-2020

GENERAL COMMENTS	The authors present the following paper: Prevalence and trends of sarcopenia metrics and related body composition: data from NHANES 1999-2006. This is an important topic; however, in its current presentation it deserves some important changes in order to avoid confusion and biased conclusions in a very changing concept. First of all, from my understanding and following sarcopenia definition since 1989, 2010 and 2018. The paper revised is not about sarcopenia syndrome. Using the 2010 EWGSOP sarcopenia criteria, the correct term that authors must be use is presarcopenia, or all related to loss of skeletal muscle component. Therefore, the introduction should be restructure focusing only in skeletal muscle, i.e. risk factors for loss of skeletal muscle, clinical implications about the loss of this body composition component. But more importantly, I would like to read, about the link between skeletal muscle in the context of obesity across NANHES surveys 1999-2006. I guess that prevalence of presarcopenia should be increased as BMI categories increases (cytokines or/and insulin resistance associated to obesity and skeletal muscle). Are there any relationships between prevalence and trends of presarcopenia by nutritional status considering BMI? Table 2 In other words, what is the possible negative impact of obesity defined by BMI, but more important defined by fat mass index (fat mass index, Kelly LT, 2009) on skeletal muscle by using DXA-fat mass derived? Nutritional status by BMI 1990-2000 2001-2002 18.4 ? ? 18.5 to 24.9 ? 25. 29.9 ? 30 ? When authors define presarcopenia, please check out the cut-off points for low skeletal muscle, the values reported of 7.26 and 5.5 did not arose from a representative sample in USA. Table 3. Be aware that weight, BMI, overweight and obesity, WC, are no body composition parameters. Finally, authors should define a system of hypothesis, one related with presarcopenia, the second ones with body composition and the last one with cardiovascular fitness. It was not clear for me the relevance of cardiovascular fitness. I was very confused about logistic regression analysis.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Leo Westbury
Institution and Country: MRC Lifecourse Epidemiology Unit, University of Southampton, UK
Please state any competing interests or state 'None declared': None declared

Dear Authors,
Below are my comments about this paper.

(1) *In the abstract, I would recommend the following: define 'NHANES'; change the phrases 'youth-orientated tendency' and 'reverse tendency' as they are a little unclear; and mention the statistics for non-Hispanic white participants in the results as they are mentioned in the conclusion.*

Re: Thanks a lot for your suggestions. We have defined the "NHANES" in the abstract (page: 3, line: 36). The phrases "*youth-orientated tendency" and "reverse tendency"* were revised as "a trend toward youth" and "has an increasing trend over time", respectively. (page: 3, line: 53-54)

(2) *It states that the prevalence of sarcopenia among adults aged 55 years and older is high (page 4, line 15). It would be helpful for the reader if this prevalence was stated.*

Re: Thanks for your comments. As your suggestion, we have added the prevalence of sarcopenia in the manuscript (page: 5, line: 75-78).

(3) *It states that loss of muscle can lead to a higher metabolic rate which can result in fat gain (page 4, lines 24-29). Shouldn't this read as 'lower metabolic rate'?*

Re: Thank you for pointing this out. We have corrected "higher resting metabolic rate" as "lower metabolic rate" for friendly reading. (page: 5, line: 88)

(4) *I feel that the introduction could explain the condition of sarcopenic obesity which can have more serious health implications than either of these two conditions in isolation. The introduction could also outline that there are a variety of sarcopenia definitions but no consensus definition.*

Re: The condition of sarcopenic obesity has been explained (page: 5, line: 93-94). We also outlined the variety of and staging of sarcopenia in the "Introduction" section (page: 5, line: 81-82).

(5) *In the section 'Study design and participants', the number of participants included in the NHANES III cohort and in the analytical sample could be stated.*

Re: We have added the sample size in each cycle survey in the section "Study design and participants" (page: 6, line: 113-115).

(6) *Only low appendicular skeletal muscle mass is used to define sarcopenia (page 5, line 58). However, the cited paper (reference 30) recommends the presence of low muscle mass and low muscle function (strength or physical performance) to define sarcopenia. Please justify why you are describing this condition as sarcopenia when it is really just a measure of muscle mass adjusted for height.*

Re: Thanks for your valuable comments. We agree that low appendicular skeletal muscle mass is one of the three components to define sarcopenia. Accordingly, we used "pre-sarcopenia" to instead of "sarcopenia" based on the reference 30 in the manuscript. (page: 7, line: 127-129)

(7) *Please explain how the variables for heart rate, VO2 max and CVD fitness were ascertained and defined.*

Re: We have added the measurement of heart rate (page 7, line 134-138), VO2 max (page: 7, line: 138-140) and CVD fitness (page: **7, line: 131-134).**

(8) *It states that in 1999-2000 (n=9), 49.6% were women. What does 'n=9' mean in this context?*

Re: We have checked the data and found that it's a clerical mistake. We have deleted "(n=9)". To eliminate potential similar problems, we have rechecked all data in the manuscript. (page: 9, line: 176-181)

(9) *Some non-significant trends are described as increases and some are described as remaining stable (Page 9, lines 5-28). It would be helpful for the reader if these were described consistently.*

Re: Good suggestions. We have revised the descriptions as "stable" for all non-significant trends consistently throughout the manuscript.

(10) *It states that participants who had high education levels were more likely to have a lower prevalence of sarcopenia compared to the lowest category of education (page 9, lines 35-40). However, I don't think this was the case in 1999-2000.*

Re: Thank you for pointing this out. We have revised the descriptions precisely according to the statistical results.

(11) It states that obesity prevalence significantly increased from 21.9% to 24.0% in the 18-39 group but then a non-significant p-value is stated (page 11, line 24). Please clarify.

Re: Thanks. We have revised the descriptions precisely according to the statistical results. (page: 15, line: 222-224)

(12) It states 'P for trend=0.229' among women and then '(all P-values for trend<0.001)' (page 11, line 19). These two statements seem to contradict each other.

Re: We have checked the data and found that it's a clerical mistake. We have corrected the errors. To eliminate potential similar problems, we have rechecked all data in the manuscript. (page: 15, line: 217-221)

(13) It states that similar trends of obesity prevalence were observed in non-Hispanic whites and Mexican Americans (Page 11, lines 28–33). Please clarify as the first group shows a significant increasing trend and the latter shows no significant trend.

Re: Thanks. We have revised the descriptions precisely according to the statistical results. (page: 15, line: 224-227)

(14) It states there was a large reduction in ASM and SMI (Page 11, lines 35–38). I don't think this supports the results in Table 3 or Figure 2A.

Re: Thanks. We have revised the descriptions precisely according to the statistical results. (page: 15, line: 227-229)

(15) It states that there were not significant sex differences over time in relation to sarcopenia prevalence (page 13, line 58). However, Table 2 shows significant sex differences in 2005-2006.

Re: Thanks. We have corrected the presentation according to the statistical results. (page: 12, line: 196-197)

(16) In the discussion, there is a statement that sarcopenia prevalence decreased in men but not in women and several possible reasons for this are offered (page 14, lines 3-50). This seems to contradict the results in Table 2 showing that trends over time were not significant among men or women.

Re: Thanks. We have corrected the presentation according to the statistical results. (page: 18, line: 269-27/span>1)

(17) The prevalence of sarcopenia among non-Hispanic blacks is stated as around 1% in 1999-2000, 7% in 2001-4 and then 26% in 2005-6. Such huge increases over such short durations do not seem plausible. Have you investigated reasons for this such as considerably more very old (>80 years) non-hispanic blacks being included in the sample at later years?

Re: We rechecked the data of prevalence of pre-sarcopenia among non-Hispanic blacks. The low prevalence in 1999-2000 may be due to the small number of pre-sarcopenic participants (only 36 pre-sarcopenia cases) in this category.

(18) I feel that grouping all participants 60 years of age and older into one group may mask the potentially large difference in prevalence and trends of sarcopenia between those in their early 60s and those in their late 80s. Are the patterns similar if more age bands are used within this age range?

Re: Thanks for your great comments. We have reanalyzed the results related to age by dividing age into: 18 – 39, 40 – 59, 60 – 79, and ≥ 80 years' old group in the manuscript. Besides, considering the potential influence of age and gender on the prevalence of pre-sarcopenia, we reported the prevalence of pre-sarcopenia after adjusting of age and gender in multivariate logistic regression models (see Table 2).

(19) Regarding the figures, please define abbreviations and correct '1988' in the Figure 1 Legend.

Re: Thanks a lot for your careful comments. We have corrected clerical mistake. (page: 26, line: 520-522)

(20) The footnotes in Table 2 state that sarcopenia was defined according to the DIA criteria. What does 'DIA' stand for?

Re: Thanks. It should be DXA, and we have presented the full spell of DXA in the foot notes in table. (page: 14, line: 211)

Reviewer: 2
Reviewer Name: ALEMAN-MATEO H
Institution and Country: Research Center for Food and Development, Hermosillo, Sonora, Mexico.

Please state any competing interests or state 'None declared': None declared

The authors present the following paper: Prevalence and trends of sarcopenia metrics and related body composition: data from NHANES 1999-2006. This is an important topic; however, in its current presentation it deserves some important changes in order to avoid confusion and biased conclusions in a very changing concept.

(1) First of all, from my understanding and following sarcopenia definition since 1989, 2010 and 2018. The paper revised is not about sarcopenia syndrome. Using the 2010 EWGSOP sarcopenia criteria, the correct term that authors must be use is presarcopenia, or all related to loss of skeletal muscle component.

Re: We are very appreciated for your useful comments. We agree that low appendicular skeletal muscle mass is one of the three components to define sarcopenia. Accordingly, we used "pre-sarcopenia" to instead of "sarcopenia" in the manuscript.

(2) Therefore, the introduction should be restructure focusing only in skeletal muscle, i.e. risk factors for loss of skeletal muscle, clinical implications about the loss of this body composition component.

Re: Thank you so much for your professional comments. According to your suggestion, we rewrote our introduction section. Currently, we focused on the skeletal muscle, not on the whole sarcopenia definition (page: 5-6, line: 71-104).

(3) But more importantly, I would like to read, about the link between skeletal muscle in the context of obesity across NANHES surveys 1999-2006. I guess that prevalence of presarcopenia should be increased as obesity increases (cytokines or/and insulin resistance associated to obesity and skeletal

muscle). Are there any relationships between prevalence and trends of presarcopenia by nutritional status considering BMI? Table 2. In other words, what is the possible negative impact of obesity defined by BMI, but more important defined by fat mass index (fat mass index, Kelly LT, 2009) on skeletal muscle by using DXA-fat mass derived? Nutritional status by BMI 1990-2000 2001-2002: 18.4 ??, 18.5 to 24.9 ?, 25. 29.9 ?, 30 ?

Re: Thanks for your comments. As you suggested, we add the results of pre-sarcopenia stratified by BMI categories over four survey cycles in Table 2. Considering the very small number of participants with BMI less than 18.5, we combined the categories of '<18.5' and '18.5 – 24.9' into one category as '<25 kg/m^2'. (see Table 1, Table 2)

(4) When authors define presarcopenia, please check out the cut-off points for low skeletal muscle, the values reported of 7.26 and 5.5 did not arose from a representative sample in USA.

Re: Thank you for your comment. Although the values of 7.26 and 5.5 were not derived from a representative sample in USA, these cut-off points are the mostly used values. The cutoff values derived by other studies were similar with these values, the range of the cutoff values were from 5.72 to 7.26 for men and from 4.51 to 6.4 for women. Although these current cutoff values were a little bit rigorous for our population, they tend to identify less presarcopenia participants and lead to a conservative conclusion. Thus, we retained the cutoff points.

(5) Table 3. Be aware that weight, BMI, overweight and obesity, WC, are no body composition parameters.

Re: Thanks a lot. We have revised the title of table 3 in order to match the contents in table properly. (page: 16, line: 236)

(6) Finally, authors should define a system of hypothesis, one related with presarcopenia, the second ones with body composition and the last one with cardiovascular fitness. It was not clear for me the relevance of cardiovascular fitness.

Re: Thank you for your good suggestion. We have reconstructed our hypothesis. Now, we only focused on the skeletal muscle and muscle related body compositions. Hope this version would be better (page: 6, line: 105-108).

(7) I was very confused about logistic regression analysis.

Re: The logistic regression analysis was conducted by 'proc surveylogistic' in SAS by considering sampling weights. We have revised the description to make it more sense and friendly-reading. (page: 8, line: 163-166)

VERSION 2 – REVIEW

REVIEWER	Leo Westbury MRC Lifecourse Epidemiology Unit, University of Southampton, UK
REVIEW RETURNED	16-Mar-2020

GENERAL COMMENTS	The phrase in the abstract stating that 'the prevalence of pre-sarcopenia has a trend toward youth', is a little unclear as it may suggest pre-sarcopenia is more common among young people, rather than the prevalence simply increasing over time among young people. The statistics on the prevalence of pre-sarcopenia and sarcopenia

	are from an Iranian study of around 300 individuals (page 6, lines 76-77). I feel that it would be more appropriate to state these statistics from a larger US or Western cohort to match the population of interest in your manuscript. It states that interactions between different groups were compared using chi-square tests (page 9, lines 162-163). This implies that interactions effects were explored when it appears that these tests were just use to examine whether participant characteristics differed according to pre-sarcopenia status (yes/no). It states that the overall age- and sex-adjusted prevalence of pre-sarcopenia ranged from 16.4% (95% CI: 18.1%, 21.4%) in 1999-2000 to 14.8% (95% CI: 14.9%, 20.2%) in 2005-2006 (page 13, lines 190-191). These confidence intervals do not seem to agree with those stated in Table 2. Please clarify '- -' in table footnotes. Table 2 helpfully states how the p-values for trend were calculated. I feel that the method for calculating the other p-values in this table could also be included in the footnotes. The adjustments used for calculating the p-values for trend as stated in the footnotes of Table 2. I feel that these adjustments should be stated in the section 'Statistical analyses'. '96% CI' is stated on the axis of Figure 1A which should be corrected. In the footnotes for Figure 1 and Figure 2, it would be helpful to state the adjustments used in the logistic regression models; these adjustments could also be stated in the section 'Statistical analyses'. I don't think 20 years of data was used for this study (page 18, line 245). It states that there were no significant sex differences over time in relation to sarcopenia prevalence (page 19, line 269-270). However, Table 2 shows significant sex differences in 2005-2006. The following phrase is a little unclear and could be clarified: 'there was a youth tendency on prevalence of pre-sarcopenia from 1999 to 2006' (page 21, line 321). The second paragraph of the discussion explains how obesity may increase the risk of pre-sarcopenia and sarcopenia and suggests that this may be a reason for the increase in pre-sarcopenia among young people in NHANES. This does not seem to support the statistics in Table 2 which show that the prevalence of pre-sarcopenia is lower among overweight and obese individuals. Therefore, I feel that the discussion could also include the remark that sarcopenia prevalence was higher among underweight participants in this study. Please proof-read the text as there are several grammatical errors.

REVIEWER	Aleman-Mateo H Centro de Investigación en Alimentación y Desarrollo, A.C.
REVIEW RETURNED	10-Mar-2020

GENERAL COMMENTS	Importantly, NHANES is a national survey (Cross-sectional design). Please be aware about this sentence. page 4, line 35. This is an analysis study of the longitudinal data. NHANES is a survey and does not have cohort o longitudinal design. Please modify this particular sentence. Please see Page 6 line 12-15 It's well written. Page 4 line 35; same observation. Page 6 line 77; are, change by is Page 6 line 89; please delete: mechanically Page 7, Line 98; How sarcopenia increases inflammation? Page 8 Line 127 Total appendicular skeletal muscle mass (TASM), This is more accepted Page 8 Line 130, I still confuse about this section of the study, my main concern what is the contribution or the relationship to this section with presarcopenia prevalencia? or obesity? or Do the author want to explore the relationship between VO2 and Physical activity? Results Page 13 Line 192 Please review the sentence from my point of view; statistically, results did not change significantly. Page 13 Line 196 there was a decreasing; however, statistically this decreases does not rich significance. Page 13 Line 204 What is the OR? Considering the results section What is the main message, obesity increased while sarcopenia decreased and in non-hispanic blacks sarcopenia increase but obesity remain stable? What king of messages we can draw?. Page 5 or 6 Line 92-93. Obesity and sedentary lifestyle play key roles in the development of age-related muscle. It seems, theta the results of present analysis does not support this. Line 96-97; Therefore, it is reasonable to hypothesize that the prevalence of pre-sarcopenia has increased. In the discussion section both sentences mus be discussed and supported by the analysis. Discussion Page 18 Line 249-250, As anticipated, pre-sarcopenia and its metrics increased accordingly in young people. Results does not support this sentence. Line 258-259. The peak period of skeletal muscle mass is around 20 years old which begins to decreases at around 30 years old. This is not true, please review the elegant paper published by Janssen I, 2000. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr In the discussion section, all discussion about muscle strength does not have sense in this context. Please check the conclusion, authors are sending other messages, please review carefully.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

1.*The phrase in the abstract stating that 'the prevalence of pre-sarcopenia has a*

trend toward youth', is a little unclear as it may suggest pre-sarcopenia is more common among young people, rather than the prevalence simply increasing over time among young people.
RE: Thank you, we have revised as your suggestion.

2. *The statistics on the prevalence of pre-sarcopenia and sarcopenia are from an Iranian study of around 300 individuals (page 6, lines 76-77). I feel that it would be more appropriate to state these statistics from a large larger US or Western cohort to match the population of interest in your manuscript.*
RE: Thanks for pointing this out. We have replaced this study with a recent published data from the general population using the European Working Group on Sarcopenia in Older People (EWGSOP) which included 5911 subjects with a mean age of 69.2 years (55.8% female).

3. *It states that interactions between different groups were compared using chi-square tests (page 9, lines 162-163). This implies that interactions effects were explored when it appears that these tests were just use to examine whether participant characteristics differed according to pre-sarcopenia status (yes/no).*
RE: No, in actually, we did not provide the results of interaction. We have deleted this sentence. Sorry for our mistaken of the presentation.

4. *It states that the overall age- and sex-adjusted prevalence of pre-sarcopenia ranged from 16.4% (95% CI: 18.1%, 21.4%) in 1999-2000 to 14.8% (95% CI: 14.9%, 20.2%) in 2005-2006 (page 13, lines 190-191). Theses confidence intervals do not seem to agree with those stated in Table 2.*
RE: Thanks for your careful comment. We have rechecked all data in the results and all tables and figures to avoid the inconsistent data and typos.

5. *Please clarify '- -' in table footnotes.*
RE: This has been well taken. Thanks.

6. *Table 2 helpfully states how the p-values for trend were calculated. I feel that the method for calculating the other p-values in this table could also be included in the footnotes.*
RE: All methods of *P*-values for groups and trends were provided at the footnotes. Thanks.

7. *The adjustments used for calculating the p-values for trend as stated in the footnotes of Table 2. I feel that these adjustments should be stated in the section 'Statistical analyses'.*
RE: This has been well taken.

8. *'96% CI' is stated on the axis of Figure 1A which should be corrected. In the footnotes for Figure 1 and Figure 2, it would be helpful to state the adjustments used in the logistic regression models; these adjustments could also be stated in the section 'Statistical analyses'.*

RE: We have added the statements both in the statistical method section and figure legends. Thank you.

9. *I don't think 20 years of data was used for this study (page 18, line 245).*
RE: This typo has been well taken. Thank you!

10. *It states that there were no significant sex differences over time in relation to sarcopenia prevalence (page 19, line 269-270). However, Table 2 shows significant sex differences in 2005-2006.*
RE: This inconsistent statement has been revised. Thank you again for your careful comment.

11.*The following phrase is a little unclear and could be clarified: 'there was a youth tendency on preva lence of pre-sarcopenia from 1999 to 2006' (page 21, line 321).*
RE: This sentence has been changed as "the prevalence of pre-sarcopenia were increased from 1999 to 2006 among U.S. young adults."

12.*The second paragraph of the discussion explains how obesity may increase the risk of pre-sarcopenia and sarcopenia and suggests that this may be a reason for the increase in pre-sarcopenia among young people in NHANES. This dose not seem to support the statistics in Table 2 which show that the prevalence of pre-sarcopenia is lower among overweight and obese individuals. Therefore, I feel that the discussion could al so include the remark that sarcopenia prevalence was higher among underweight participants in this study.*
RE: Thanks a lot for your careful comment. We discussed the result that the sarcopenia prevalence was higher among underweight/normal weight participants in the second paragraph of the discussion section.

13. *Please proof-read the text as there are several grammatical errors.*
RE: As your suggestion, we invited a professional language editor from AJE to help us to proof-read the whole manuscript. All authors have read the whole manuscript to double check the grammatical errors. Hope this version could fulfill your requirement.

Reviewer: 2

1. *Importantly, NHANES is a national survey (Cross-sectional design). Please be aware about this sentence. Page 4, line 35. This is an analysis study of the longitudinal data. NHANE S is a survey and does not have cohort or longitudinal design. Please modify this particular sentence.*

RE: Thank you for your comment. We have replaced the longitudinal design with cross-sectional design.

2. *Please see Page 6 line 12-15 It's well written.*
3. *Page 4 line 35; same observation.*

RE: Thank you!

4. *Page 6 line 77; are, change by is*
5. *Page 6 line 89; please delete: mechanically*

RE: All these have been well taken. Thanks!

6. *Page 7, Line 98; How sarcopenia increases inflammation?*

RE：Thanks for your comments. Although the underlying mechanism is unknown, evidence suggests that there might be an association between sarcopenia and inflammation. Several health studies suggested that circulating inflammatory factors, such as IL-6 and TNF-*α*, were significantly higher among sarcopenic elderly. Also, the elevated IL-6 and CRP related with high risk of muscle strength loss. Moreover, it is reported that low muscle mass is associated with increased postoperative inflammation in patients undergoing colorectal cancer surgery.

7. *Page 8 Line 127 Total appendicular skeletal muscle mass (TASM), This is more accepted*

RE: Thank you. All “skeletal muscle mass” were changed as “Total appendicular skeletal muscle mass (TASM)”.

8. *Page 8 Line 130, I still confuse about this section of the study, my main concern what is the contribution or the relationship to this section with presarcopenia prevalencia? or obesity? or Do the author want to explore the relationship between VO2 and Physical activity?*

RE: Thank you for your comment. The primary aim is the pre-sarcopenia prevalence and obesity. As your comment, we have deleted all specific results of cardiovascular fitness.

Results

9. *Page 13 Line 192 Please review the sentence from my point of view; statistically, results did not change significantly.*

10*. Page 13 Line 196 there was a decreasing; however, statistically this decreases does not rich significance.*

RE: We have revised all these sentences accordingly. Thanks.

11. *Page 13 Line 204 What is the OR?*

RE: We did not calculate the OR values. Using the logistic regression models, we aimed to test whether there was an increase or decrease trend in the prevalence of pre-sarcopenia over the survey period. We have detailed the method in the statistical method section and cited the references.

Considering the results section

12. *What is the main message, obesity increased while sarcopenia decreased and in non-Hispanic blacks sarcopenia increase but obesity remain stable? What kind of message we can draw?*

RE: Thanks a lot for your valuable comments. We think that the main findings in our study include: 1) the overall prevalence of pre-sarcopenia remains stable, while there is a significant increase in young adults and non-Hispanic blacks from 1999 to 2006. 2) Adults who were elderly or under/normal weight were high risk subpopulation of pre-sarcopenia. 3) Prevalence of obesity and central obesity significantly increased from 1999 to 2006. We have revised the abstract and conclusion parts correspondingly.

13. *Page 5 or 6 Line 92-93. Obesity and sedentary lifestyle play key roles in the development of age-related muscle. It seems, that the results of present analysis does not support this.*

RE: Thanks a lot for your careful comments. Actually, our results found that adults who reported vigorous physical activity had lower prevalence of pre-sarcopenia as compared to those with moderate or below physical activity, but not true for obesity. However, we deleted this weak argument in the manuscript, and focus our statements on sarcopenic obesity.

14. *Line 96-97; therefore, it is reasonable to hypothesize that the prevalence of pre-sarcopenia has increased. In the discussion section both sentences must be discussed and supporte d by the analysis.*

RE: Thanks a lot for your comments. We have revised all these discussions accordingly.

Discussion

15. *Page 18 Line 249-250, As anticipated, pre-sarcopenia and its metrics increased accordingly in young people. Results does not support this sentence.*

RE: Thank you. We have carefully reviewed the results and revised the key findings in the manuscript. The aforementioned statement is not clearly supported by the main results. Therefore, we deleted this sentence. The descriptions of key findings in the first paragraph of discussion part is revised accordingly.

16. *Line 258-259. The peak period of skeletal muscle mass is around 20 years old which begins to decreases at around 30 years old. This is not true, please review the elegant paper published by Janssen I, 2000. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr*

RE: Thanks a lot for your valuable comments. We have revised the arguments according to the mentioned reference.

17. *In the discussion section, all discussion about muscle strength does not have sense in this context.*

RE: Thanks a lot. We agreed with your comments. As our study only measured the skeletal muscle mass rather than muscle strength, and pre-sarcopenia was defined based on the measures of skeletal muscle mass, we weaken the statement related to muscle strength.

18. *Please check the conclusion, authors are sending other messages, please review carefully.*

RE: We have amended the conclusion part clearer according to the key findings of our manuscript.

VERSION 3 – REVIEW

REVIEWER	Leo Westbury MRC Lifecourse Epidemiology Unit, University of Southampton, UK
REVIEW RETURNED	06-May-2020

GENERAL COMMENTS	Many thanks for revising the paper in light of my suggestions. I just have a couple of further suggestions: The increasing trend in pre-sarcopenia among non-Hispanic black participants is robust to adjustment as shown in Table 2. However,

	the actual prevalence among this group in 2005-2006 (20.6% [95% CI: 13.0%, 31.1%]) is probably unreliable, reflected by the wide confidence interval (suggesting it is based on small numbers of participants) and the unfeasible increase of around 2.5 fold from only 8.6% in 2003-2004. Therefore, in the results section of the abstract, it may be better to mention the significant increasing trend but not to state the actual prevalences of pre-sarcopenia in this group. The following sentence is stated in the conclusion: 'Meanwhile, we found a significant increased trend of obesity, central obesity, and pre-sarcopenia in non-Hispanic blacks and young adults.' This may imply that the increasing trend of obesity and central obesity was only among non-Hispanic blacks and young adults whereas I think this was among the whole sample. Please clarify this.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 1

The increasing trend in pre-sarcopenia among non-Hispanic black participants is robust to adjustment as shown in Table 2. However, the actual prevalence among this group in 2005-2006 (20.6% [95% CI: 13.0%, 31.1%]) is probably unreliable, reflected by the wide confidence interval (suggesting it is based on small numbers of participants) and the unfeasible increase of around 2.5 fold from only 8.6% in 2003-2004. Therefore, in the results section of the abstract, it may be better to mention the significant increasing trend but not to state the actual prevalences of pre-sarcopenia in this group.

RE: Thanks for your careful comment and suggestion. As your suggestion, we revised the abstract on Page 3 lines 50-52.

The following sentence is stated in the conclusion: 'Meanwhile, we found a significant increased trend of obesity, central obesity, and pre-sarcopenia in non-Hispanic blacks and young adults.' This may imply that the increasing trend of obesity and central obesity was only among non-Hispanic blacks and young adults whereas I think this was among the whole sample. Please clarify this.

RE: Totally agree! Thank you for pointing this out. This sentence has been changed as "Meanwhile, we found a significant increased trend of obesity, central obesity." (Page 20, lines 318-320)

VERSION 4 – REVIEW

REVIEWER	Leo Westbury MRC Lifecourse Epidemiology Unit, University of Southampton, UK
REVIEW RETURNED	12-Jun-2020

GENERAL COMMENTS	Many thanks for modifying the paper in light of my comments. I have no further suggestions.