PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Physical activity, sedentary time and their associations with clustered metabolic risk among people with type 2 diabetes in Jiangsu Province: A cross-sectional study
AUTHORS	Chen, Yijia; Yang, Jie; Su, Jian; Qin, Yu; Shen, Chong; Li, Ying; Shurong Lv, Lv; Pan, Enchun; Gao, Yan; Miao, Dandan; Zhang, Ning; Zhou, Jinyi; WU, Ming

VERSION 1 - REVIEW

REVIEWER	Antje Ullrich University Medicine Greifswald, Institute of Social Medicine and Prevention, Germany
REVIEW RETURNED	08-Feb-2019

GENERAL COMMENTS	Thank you for giving me the opportunity to review this manuscript. This cross-sectional study examined the associations of physical activity (PA) and sedentary time (ST) with clustered metabolic risk in a large sample of community-managed type 2 diabetes patients in China. Although the study seems to be well described and conducted, the analytical approach to solve the research question seems to be improper, and needs to be clarified. Furthermore, the main conclusions of the study need to be highlighted. A number of revisions, some of them of major importance, are suggested to aid clarity and readability; furthermore, the introduction, methods and discussion require more extensive revision. Thus, there are some clarifications required in order to accept this manuscript. I detailed my comments and suggestions below: Major compulsory revisions Introduction

	• It is stated that there is not much evidence about joint associations between PA and ST with clustered metabolic risk or/and individual metabolic risk factors. In fact, there are a growing number of studies that have examined joint associations between PA and ST and cardiometabolic factors or risk scores. It might be useful to the readers and appropriate to add an overview of cross-sectional (i.e., Healy et al., 2008; Wagner et al., 2012; Petersen et al., 2014) as well as longitudinal studies (i.e., Shuval et al., 2014; Knaeps et al., 2016; Lamb et al., 2016) that have analyzed PA and ST with cardiometabolic outcomes in the Introduction section. Please revise. • In light of the fact that this study has examined the associations of PA and ST with the clustered cardiometabolic risk in an Asian population, it seems important to report how these behaviors could differ from those in Western populations. This aspect could be introduced more thoroughly and it would also be relevant as a limitation/discussion point. Methods • There is evidence that the context in which people sit or are active is relevant in terms of cardiometabolic risk. The authors used an instrument (GPAQ) to assess several types of PA and therefore, they might be able to provide a more complete impression of PA than if they use the average PA. Did the authors consider analyzing context-specific aspects of PA with cardiometabolic risk? Being active at work, getting to work or being active in leisure time seems to be different, and moreover, a person can change that behavior in other ways ... • In the literature, there are different ways to calculate clustered cardiometabolic risk. Regarding the significant gender differences in almost all of the cardiometabolic variables shown in Table 1, each cardiometabolic variable can be standardized by using gender-specific sample means and standard deviations. Therefore, gender differences can be considered. • In addition, sex and age were included as covariates in the analysis, but did the authors observe any gender-specific or age-specific interactions (Figure 1 suggests this)? If so, it seems relevant to stratify results on gender or/and age. The aspect of gender-specific or/and age-specific patterns of PA and ST could also be relevant as a limitation/discussion point. • I suggest the authors use S Table 4 instead of Table 3 and, therefore, include sleep as a relevant covariate in the main analysis (possibly as Model 3), not just in a sensitivity analysis. As the authors stated in the Introduction section "When exploring the associations of physical activity and sedentary time with metabolic risk factors, it is crucial to elucidate whether this association is independent of sleep duration, which might confound the association with metabolic risk.". In addition, I suggest to eliminate the second sensitivity analysis (use BMI and DBP instead of WC and SBP) from the manuscript, since this analysis, in my opinion, hardly contributes to the results. Results • It is stated that excluded and included participants differ significantly in terms of waist circumference and systolic

	blood pressure. It would be important to discuss these results in the limitation/discussion section. • In Figure 1, the authors present results of a gender-specific analysis of the association of PA and ST with zMs. Please give rationale for the cut-off values of PA (<5MET h/d) and ST (>5 h/d) and specify the cut-off values they have used to differentiate between light, moderate, and high PA and ST values. However, it is also important to include a section in the Method section for this analysis. • Forgive me if I am misunderstanding, but I cannot find the results of the sensitivity analysis of replacing WC and SBP with BMI and DBP and the results of the calculation of the new clustered metabolic score (without waist circumference) in the S Table 4. Discussion • The paper would clearly benefit if the authors could discuss possible implications of the study results for future studies. It is stated that a "more detailed relationship between different pattern of physical activity and sedentary time with metabolic risks need to be explored". Please, discuss this further. • It might be useful to add further discussion about the limitation… • of using self-report questionnaire in this study. Self-report assessments are sensitive to recall bias as well as social desirability. Further, correlations between accelerometry and self-report questionnaires are weak to moderate. A review of Skender et al. (2016) recommended – especially for measuring sedentary time – a combined use of questionnaires and accelerometers in order to receive the most comprehensive information. * Skender S, Ose J, Chang-Claude J, et al. Accelerometry and physical activity questionnaires - a systematic review. BMC Public Health. 2016;16:515. • on the representativeness/generalizability of the findings to the population as a whole. • Finally, I thought the implications for policy and practice needed much more detail. Minor essential revisions Abstract • Please state the results of glucose in the Abstract section as well. Introduction • The paragraph of the definition of the metabolic syndrome is similar in the Introduction and in the Method section. The authors could eliminate the paragraph in the Introduction section. • I suggest to add "maintaining or"* to the sentence "The increasing prevalence and serious health consequences suggested that preventive strategies for * improving metabolic health should be required.". • The following sentence is unclear: "However, most studies focused on risk associated with lack of physical rather than sedentary time." Please clarify. • Please clarify why: "In addition, the increasing evidence have suggested that use the continuous summary score of clustered metabolic risk (zMS) in analyses, instead of a

	binary definition dichotomizing continuous outcome variables, which improve statistical power to detect associations." • At the end of the intro, the authors might state the scientific hypothesis of this study (what kind of results do the authors expect?). Methods • It is stated that "spending more than 16 hours on daily physical activity" is an exclusion criterion. Please clarify why. • I suggest the authors to eliminate "during the past years" in the sentence "Information on physical activity and sedentary time during the past years was collected by using Global Physical Activity Questionnaire (GPAQ).". • Sleep is missing as covariate in the Covariate definition section. • Did the authors collect information on hypertension medication? If an antihypertensive medication was taken, it seems relevant to adjust for these treatment effects – especially for systolic blood pressure (Tobin et al., 2005). * Tobin MD, Sheehan NA, Scurrah KJ, Burton PR. Adjusting for treatment effects in studies of quantitative traits: antihypertensive therapy and systolic blood pressure. Stat Med. 2005;24(19):2911–35. https://doi.org/10.1002/sim.2165. • Please provide information on the normality of variables and residuals (homoscedasticity, linearity, independence) in the statistical section. Please also provide information on the multicollinearity of the variables (variance inflation factor) in the regression models. • Please report the cut-off values of the adiposity component that was used in the sensitivity analysis. Results • Some information of the main text is already on tables (i.e. Table 1) which should be avoided – see the first paragraph of the results section. • As shown in Table 1, the average age is relatively high (M = 62.76). This is probably due to the diabetes population the study is focusing on, right? Did the authors consider setting the age range from 40/45 years? Since PA and ST patterns differ among younger, middle, and older individuals, an age-specific analysis is required, or this topic should be discussed in the Discussion section. • As shown in Table 2, metabolic variables showed a significant overall difference depending on the quartiles of PA and ST. It is important to know which quantile groups are different. Therefore, please provide the results of the corresponding post hoc tests. • I am a little confused about the different regression models, the authors present in the results section. It is stated in Table 3 that all models are adjusted for age, sex, etc. – even the crude model or just Model 1? Please clarify this in the legend of the table as well as in the Methods section. • I suggest the authors eliminate the Table S3 from the manuscript. PA, sitting, and sleeping are behaviors that exclude each other, therefore, a low correlation between this variables are to be expected. Discussion • Please expand a little further on the potential implications of the results that ST and glucose correlate significantly in this

	study. Which possible biological mechanism could be responsible for the results? (Ceriello et al., 2000; Heine et al. 2004) * Ceriello A. The post-prandial state and cardiovascular disease: relevance to diabetes mellitus.Diabetes Metab Res Rev. 2000; 16:125–132. Heine RJ, Balkau B, Ceriello A, Del Prato S, Horton ES, Taskinen MR. What does postprandial hyperglycaemia mean?Diabet Med. 2004; 21:208–213. • Sedentary behavior and physical activity patterns have been shown to vary between weekends and weekdays, because weekday ST activities and PA are likely to be more routine than at weekends. This would be relevant to discuss in regard of future studies. • Results of a recent study suggest that there is limited evidence linking sitting and incident diabetes over 13 years (adjusted for moderate-to-vigorous physical activity and BMI) (Stamatakis et al., 2017). Therefore, please expand the discussion section on the potential impact of your study results. * Stamatakis E, Pulsford RM, Brunner EJ, et al. Sitting behaviour is not associated with incident diabetes over 13 years: the Whitehall II cohort study. Br J Sports Med 2017;51:818-823. Conclusion • I suggest the authors eliminate “lack of” and “excess” from the following sentence: “Our results suggest that lack of physical activity and excess sedentary time are both independently associated with clustered and individual metabolic risk in community type 2 diabetic patients.” Discretionary Revisions • The manuscript requires professional English editing.

VERSION 1 – AUTHOR RESPONSE

Reviewer' comments and point-to-point responses:

Reviewer #1: This cross-sectional study examined the associations of physical activity (PA) and sedentary time (ST) with clustered metabolic risk in a large sample of community-managed type 2 diabetes patients in China.

Although the study seems to be well described and conducted, the analytical approach to solve the research question seems to be improper, and needs to be clarified. Furthermore, the main conclusions of the study need to be highlighted. A number of revisions, some of them of major importance, are suggested to aid clarity and readability; furthermore, the introduction, methods and discussion require more extensive revision. Thus, there are some clarifications required in order to accept this manuscript. I detailed my comments and suggestions below:

Major compulsory revisions

1. Introduction

Q1. - It is stated that there is not much evidence about joint associations between PA and ST with clustered metabolic risk or/and individual metabolic risk factors. In fact, there are a growing number of studies that have examined joint associations between PA and ST and cardiometabolic factors or risk scores. It might be useful to the readers and appropriate to add an overview of cross-sectional (i.e., Healy et al., 2008; Wagner et al., 2012; Petersen et al., 2014) as well as longitudinal studies (i.e., Shuval et al., 2014; Knaeps et al., 2016; Lamb et al., 2016) that have analyzed PA and ST with cardiometabolic outcomes in the Introduction section. Please revise.

Re: Thank you for your advice. We have read the relevant cross-sectional and longitudinal studies carefully and some representative researches were cited (Reference [15] and [16]) in the Introduction section of this manuscript. We also have eliminated this unclear expression in revised manuscript (“ It is stated that there is not much evidence about joint associations between PA and ST with clustered metabolic risk or/and individual metabolic risk factors.”)

Q2. - In light of the fact that this study has examined the associations of PA and ST with the clustered cardiometabolic risk in an Asian population, it seems important to report how these behaviors could differ from those in Western populations. This aspect could be introduced more thoroughly and it would also be relevant as a limitation/discussion point.

Re: We thank the reviewer for the suggestions. It was reported that the proportion of adult Chinese participating in leisure-time physical activity was rather low (~20%) (Ng et al., Soc Sci Med 2009), and much lower than that observed in Western populations (typically ~70%) (Haskell et al., Circulation 2007). We reported the main difference of physical activity behaviors between Chinese and Western populations in the Page 3 and discussed it in Page 14.

Page 3, paragraph 2:-“Most of them emphasized the value of assessing overall physical activity or leisure-time physical activity, but few have focused on other domains of physical activity (e.g. occupational, household or commuting). Evidence showed that information on different domains of physical activity may be crucial for Chinese people because they were found with quite different patterns of physical activity compared with their Western counterparts. For example, it was reported that occupational and household activities contributed substantially more to total physical activity than leisure time or transportation activity did.”

Page 14, paragraph 2: -“Importantly, we observed that occupational physical activity reduces the clustered metabolic risk in patients with type 2 diabetes. Occupational physical activity is a major source of total physical activity for Chinese people and other Asian populations (In this study, 75.8% of patients with diabetes reported engaging in occupational physical activity.) This finding suggested a special importance of occupational physical activity as a single domain for the management of metabolic risk among Chinese people or even broadly among Asian populations. Though there was a trend for lower levels of commuting physical activity to be associated with higher metabolic risk in recent study, there was no statistically significant association observed between commuting physical activity and clustered metabolic risk in this study, which is similar to the finding of the J-ECOH Study. This may partly be explained that the level of commuting physical activity is low in our study.”

2. Methods

Q3. -There is evidence that the context in which people sit or are active is relevant in terms of cardiometabolic risk. The authors used an instrument (GPAQ) to assess several types of PA and therefore, they might be able to provide a more complete impression of PA than if they use the average PA. Did the authors consider analyzing context-specific aspects of PA with cardiometabolic risk? Being active at work, getting to work or being active in leisure time seems to be different, and moreover, a person can change that behavior in other ways.

Re: Thank you for pointing this out. Considering differences of physical activity behaviors between Chinese and Western populations, it is essential to examine whether the association between physical activity domains and cardiometabolic risk among Chinese people differs from those in Western populations. Thus, we extended the results to occupational, commuting and leisure-time physical activity in Table 3 (please see Page 27 and 28) and Table S3, which are also of the key results of this study.

Q4. - In the literature, there are different ways to calculate clustered cardiometabolic risk. Regarding the significant gender differences in almost all of the cardiometabolic variables shown in Table 1, each cardiometabolic variable can be standardized by using gender-specific sample means and standard deviations. Therefore, gender differences can be considered.

Re: Thank you for this suggestion. We constructed a continuous variable by summing up the gender-specific standardized values for waist circumference, fasting triacylglycerol, fasting plasma glucose, systolic blood pressure and the inverse of HDL-cholesterol. Relevant contents were provided in Page 7 in the revised manuscript. All results related to zMS have been updated accordingly.

Page 7, paragraph 1: - “Each of these variables was standardized by subtracting the gender-specific sample means from the individual mean and dividing by the standard deviations (SD)”

Q4. -In addition, sex and age were included as covariates in the analysis, but did the authors observe any gender-specific or age-specific interactions (Figure 1 suggests this)? If so, it seems relevant to stratify results on gender or/and age. The aspect of gender-specific or/and age-specific patterns of PA and ST could also be relevant as a limitation/discussion point.

Re: Thank you for your recommendation. Stratified analyses by sex and age were performed in Table S3. We divide the age variable into 4 categories (＜55, 55~, 65~ and ≥ 75 years). In addition, interactions between main predictor variables with sex and age were examined by entering the centered interaction terms regression models (Aiken and West, 1991). We found that the association between ST, total and occupational PA with zMS and waist circumference were modified by age, but no significant interactions by sex were observed. Relevant method and results were provided in Page 9-10, Page 13 and Table S3. Furthermore, the discussion about these results have been added in Page 16 in this manuscript.

Page 9-10, paragraph 2:- “Interactions between the main predictive variables with sex and age (continuous) were examined by entering the centered interaction terms in multivariate linear regression models. Interactions examined whether the association between physical activity and sedentary time with the total and individual subcomponents of zMS were modified by sex and age. ”

Page 13, paragraph 2:- “Interaction analyses indicated significant effects among different age groups, greater associations of sedentary time, total and occupational physical activity with zMS (P for interaction <0.10) and waist circumference (P for interaction <0.05) were observed among older age groups. In addition, there was no significant interaction for sex in the results of total physical activity, different domains of physical activity or sedentary time.”

Page 16, paragraph 1:-“We also found that relationship between sedentary time with zMS and waist circumference was modified by age. This may partly due to time spent in sedentary behavior increased with age. Older patients may at a higher risk of clustered metabolic risk than younger people based on this age-related increase of sedentary time.”

Q5. - I suggest the authors use S Table 4 instead of Table 3 and, therefore, include sleep as a relevant covariate in the main analysis (possibly as Model 3), not just in a sensitivity analysis. As the authors stated in the Introduction section “When exploring the associations of physical activity and sedentary time with metabolic risk factors, it is crucial to elucidate whether this association is independent of sleep duration, which might confound the association with metabolic risk.”.

In addition, I suggest to eliminate the second sensitivity analysis (use BMI and DBP instead of WC and SBP) from the manuscript, since this analysis, in my opinion, hardly contributes to the results.

Re: Thank you for your suggestion. We have included sleep duration as a relevant covariate in the main analysis (Model 4) and eliminated the second sensitivity analysis in this revision.

3. Results

Q6. - It is stated that excluded and included participants differ significantly in terms of waist circumference and systolic blood pressure. It would be important to discuss these results in the limitation/discussion section.

Re: Thank you for your recommendation. The discussion of this limitation has been added in Page 18 in the revised manuscript.

Page 18, paragraph 1:-“Second, waist circumference and systolic blood pressure of included participants were observed to be slightly higher than excluded cases, which may cause less accurate estimation of our results.”

Q7. -In Figure 1, the authors present results of a gender-specific analysis of the association of PA and ST with zMs. Please give rationale for the cut-off values of PA (<5MET h/d) and ST (>5 h/d) and specify the cut-off values they have used to differentiate between light, moderate, and high PA and ST values. However, it is also important to include a section in the Method section for this analysis.

Re: Thank you for your advice. To investigate the joint association of physical activity and sedentary time with clustered metabolic risk, participants were classified into 3 groups by sex-specific tertiles of physical activity and 4 groups by quartiles of sedentary time. Which means for physical activity, in men, the cut off values for defining low, moderate, and high tertile groups were 4.00 and 11.14 MET-h/d, whereas in women, the corresponding cutoff values were 4.57 and 12.00 MET-h/d. For sedentary time, in men, the 4 groups by quartiles of sedentary time were ＜2.2, 2.3-3.3, 3.4-4.9 and ≥5.0 h/d, whereas in women, the corresponding 4 groups were ＜2.2, 2.3-3.3, 3.4-4.4 and ≥4.5 h/d, respectively. We have recalculated the result of Figure1, and added detailed contents in Method section and legend of Figure 1.

Q8. - Forgive me if I am misunderstanding, but I cannot find the results of the sensitivity analysis of replacing WC and SBP with BMI and DBP and the results of the calculation of the new clustered metabolic score (without waist circumference) in the S Table 4.

Re: Considering the high correlation of BMI and DBP with WC and SBP, the second sensitivity analysis (use BMI and DBP instead of WC and SBP) may contribute litter to our results. So we have eliminated the second sensitivity analysis in revision manuscript.

4. Discussion

Q9. - The paper would clearly benefit if the authors could discuss possible implications of the study results for future studies. It is stated that a “more detailed relationship between different pattern of physical activity and sedentary time with metabolic risks need to be explored”. Please, discuss this further

Re: Thank you for your suggestion. The Strengths, limitations, conclusion and next steps of the study have been provided in Page 18 and Page 19 in this manuscript.

Page 18, paragraph 1: next steps of study-“Moreover, the patterns of physical activity and sedentary behaviors may vary between weekdays and weekends, but such variation is hard to be obtain by self-report measures used in the study. Further researches are needed to explore more detailed relationship between different pattern of physical activity and sedentary behavior (specifically comparing weekdays and weekends) with metabolic risks in type 2 diabetic patients.”

Page 19, paragraph 1: possible implications of the study results- “Findings from this study extend previous cross-sectional and longitudinal evidence in associations of physical activity, sedentary time and metabolic risk in the Chinese population.”

Q10. - It might be useful to add further discussion about the limitation of using self-report questionnaire in this study. Self-report assessments are sensitive to recall bias as well as social desirability. Further, correlations between accelerometry and self-report questionnaires are weak to moderate. A review of Skender et al. (2016) recommended – especially for measuring sedentary time – a combined use of questionnaires and accelerometers in order to receive the most comprehensive information.

* Skender S, Ose J, Chang-Claude J, et al. Accelerometry and physical activity questionnaires - a systematic review. BMC Public Health. 2016;16:515.…

Re: Thank you for your advice. We have read this study carefully and provided a detailed discussion about the limitation of using self-report questionnaire in Page 18.

Page 18, paragraph 1:- “Finally, we used physical activity information through a self-report questionnaire, so that reporting error may occur due to recall bias. The self-reported measures of physical activity is easier to use but may have limited validity when compared to

objective measures. Moreover, the patterns of physical activity and sedentary behaviors may vary between weekdays and weekends, but such variation is hard to be obtain by self-report measures used in the study."

Q11. - on the representativeness/generalizability of the findings to the population as a whole.

Re: The CRPCD project is a large community-based study. In brief, from December 2013 to January 2014, 29,705 registered diabetes patients in community were recruited form 44 selected townships in two areas of Jiangsu Province, China. After excluding non-T2D patients, and individuals with poor physical or mental status, a total of 20,340 subjects completed the investigation. This study was carried out in Huai'an and Changshu City in Jiangsu Province, the economic level and living habits of the two cities can comprehensively reflect characteristics of northern and southern Jiangsu Province. However, all participants were recruited from Jiangsu province. Thus, it remains to be determined whether similar findings would be obtained for patients in other regions of China. This has been discussed as a limitation in Page 18.

Page 18, paragraph 1:-"Third, all participants were recruited from two areas in Jiangsu province, China, whether the findings can be generalized to the population at large need to be discussed."

Q12. - Finally, I thought the implications for policy and practice needed much more detail.

Re: Thank you for your advice. The detailed contents were mentioned in the Page 17 in this manuscript.

Page 17, paragraph 2:- "The American Diabetes Association (ADA) recommended that type 2 diabetic patients should be assessed for conditions that might be associated with risk of cardiovascular disease before undertaking vigorous intensity exercise. Our findings also suggested that patients with type 2 diabetes should complying with the ADA recommendations to increase overall physical activity through working, active transport and participation in exercise and reduce sedentary behavior to reduce metabolic risks."

Minor essential revisions

1. Abstract

Q1. - Please state the results of glucose in the Abstract section as well.

Re: Thanks for the reminder. Data suggested that commuting physical activity and sedentary time was significantly associated with fasting plasma glucose. Relevant results of fasting plasma glucose have been added in the Abstract section (please see Page 2).

Page 2, Abstract:-“Commuting physical activity and sedentary time were significantly associated with triacylglycerol (B= -0.012; 95% CI: -0.019, -0.005) and fasting plasma glucose (B= 0.008; 95% CI: 0.003, 0.01), respectively.”

2. Introduction

Q2. - The paragraph of the definition of the metabolic syndrome is similar in the Introduction and in the Method section. The authors could eliminate the paragraph in the Introduction section.

Re: Thank you for your recommendation. The paragraph of the definition of the metabolic syndrome in the Introduction section has been eliminated.

Q3. - I suggest to add “maintaining or”* to the sentence “The increasing prevalence and serious health consequences suggested that preventive strategies for * improving metabolic health should be required.”

Re: Thank you for your suggestion. It had been added in the revised manuscript.

Q4. - The following sentence is unclear: “However, most studies focused on risk associated with lack of physical rather than sedentary time.” Please clarify.

Re: This sentence meant that when compare with physical activity, there are few studies to explore relationship between sedentary time and cardiometabolic factors. However, in fact, there are a growing number of studies that have examined associations between sedentary time and clustered metabolic risk or/and individual metabolic risk factors. So we have erased this misleading sentence.

Q5. - Please clarify why: “In addition, the increasing evidence have suggested that use the continuous summary score of clustered metabolic risk (zMS) in analyses, instead of a binary definition dichotomizing continuous outcome variables, which improve statistical power to detect associations.”

Re: Previous study (Reference [21] in the manuscript) reported that dichotomizing could leads to several problems: Firstly, information may lost as a consequence, the statistical power to detect a relation between the variable and patient outcome is reduced. Dichotomization may also increase the risk of a false positive result. Secondly, one may seriously underestimate

the extent of variation in outcome between groups, such as the risk of some events, and considerable variability may be subsumed within each group. Thirdly, using two groups conceals any non-linearity in the relation between the variable and outcome. So instead of categorizing continuous variables, we prefer keeping them continuous.

Q6. - At the end of the intro, the authors might state the scientific hypothesis of this study (what kind of results do the authors expect?).

Re: Thank you for your recommendation. The scientific hypothesis of this study has been added at the end of Introduction section (please see Page 5).

Page 5, paragraph 2:- “We hypothesized that both physical activity and sedentary time would be associated with clustered and individuals metabolic risk.”

3. Methods

Q7. - It is stated that “spending more than 16 hours on daily physical activity” is an exclusion criterion. Please clarify why.

Re: I'm sorry that we did not explain it clearly. The details of such exclusion criteria was introduced in a Chinese guideline for data processing and analysis concerning the International Physical Activity Questionnaire (Fan et al. Zhonghua Liu Xing Bing Xue Za Zhi. 2014;35: 961-964). First of all, the cumulative time of each activity every day should be converted into minutes. Assuming that each person has at least 8 hours of sleep per day, participants who reported the total cumulative time of physical activities exceeds 960 minutes (16 h) will not be included in the analysis. In our study, there were 67 subjects who reported spending more than 16 hours on daily physical activity and was not involved in the analysis.

Q8. -I suggest the authors to eliminate “during the past years” in the sentence “Information on physical activity and sedentary time during the past years was collected by using Global Physical Activity Questionnaire (GPAQ).”.

Re: Your suggestion has been adapted and the phrase of “during the past years” had been deleted from this sentence.

Q9. - Sleep is missing as covariate in the Covariate definition section.

Re: Thank you to point this out. The definition of sleep has been added in Covariate definition section in this revision (please see Page 8).

Page 8, paragraph 1:-“Sleep duration was assessed by the question “How many cumulative hours do you have for sleep on an average day?”

Q10. -Did the authors collect information on hypertension medication? If an antihypertensive medication was taken, it seems relevant to adjust for these treatment effects – especially for systolic blood pressure (Tobin et al., 2005).

* Tobin MD, Sheehan NA, Scurrah KJ, Burton PR. Adjusting for treatment effects in studies of quantitative traits: antihypertensive therapy and systolic blood pressure. Stat Med. 2005;24(19):2911–35. https://doi.org/10.1002/sim.2165.

Re: Thank you for your suggestions. We collected information on antihypertensive medication and lipid-lowing medication in this study. We additionally adjusted for the diagnosis of hypertension and use of antihypertensive medication when systolic blood pressure was the outcome of interest. For triacylglycerol and HDL-cholesterol, we adjusted for the diagnosis of dyslipidemia and use of lipid-lowering medication. Relevant contents have been added in the Statistical analysis section in the revised manuscript (please see Page 9).

Page 9, paragraph 1:-"When the dependent variable was fasting plasma glucose, we additionally adjusted for the use of glucose-lowering medication. For triacylglycerol and HDL-cholesterol we adjusted for the diagnosis of dyslipidemia and use of lipid-lowering medication. When the outcome of interest was systolic blood pressure, we additionally adjusted for the diagnosis of hypertension and use of antihypertensive medication. For zMS we adjusted for the use of medications on glucose-lowering, lipid-lowering, or antihypertensive and the diagnosis of dyslipidemia and hypertension. "

Q11. -Please provide information on the normality of variables and residuals (homoscedasticity, linearity, independence) in the statistical section. Please also provide information on the multicollinearity of the variables (variance inflation factor) in the regression models.

Re: Thank you for your advice. Information on the distribution of variables and residuals has been provided in Page 9 in the Statistical section.

Page 9, paragraph 1:-"Preliminary checks were conducted to ensure no violation of assumptions of normality, homogeneity of variance and absence of multicollinearity."

Q12. - Please report the cut-off values of the adiposity component that was used in the sensitivity analysis.

Re: We are sorry for the unclear expression. In further sensitivity analyses, in order to explore whether the associations between physical activity and sedentary time with clustered metabolic risk were mediated by adiposity, we calculated a new metabolic syndrome score without the waist circumference, which means the new metabolic syndrome score calculated by summing the gender-specific standardized values for fasting triacylglycerol, fasting plasma

glucose, systolic blood pressure and the inverse of HDL-cholesterol (standardized metabolic-risk score excluding the waist circumference). We have corrected it and we also feel great thanks for your reminder.

4. Results

Q13. - Some information of the main text is already on tables (i.e. Table 1) which should be avoided – see the first paragraph of the results section.

Re: Thank you for pointing this out. Duplicated contents in the manuscript has been removed.

Q14. - As shown in Table 1, the average age is relatively high (M = 62.76). This is probably due to the diabetes population the study is focusing on, right? Did the authors consider setting the age range from 40/45 years? Since PA and ST patterns differ among younger, middle, and older individuals, an age-specific analysis is required, or this topic should be discussed in the Discussion section.

Re: We agree with the reviewer that the relative high age is related to the population we studied. In this study, patients with type 2 diabetes aged 21-94 years old, with an average of 62.8 (9.8). The age-analysis and discussion have provided in Table S3 and Page 16, respectively.

Page 16, paragraph 1: - “This may partly due to time spent in sedentary behavior increased with age. Older patients may at a higher risk of clustered metabolic risk than younger people based on this age-related increase of sedentary time.”

Q15. - As shown in Table 2, metabolic variables showed a significant overall difference depending on the quartiles of PA and ST. It is important to know which quantile groups are different. Therefore, please provide the results of the corresponding post hoc tests.

Re: Thank you for your suggestion. Multiple comparison between groups was performed using Bonferroni method. The results have been provided in Table 2 (please see Page 26) in this manuscript.

Q16. - I am a little confused about the different regression models, the authors present in the results section. It is stated in Table 3 that all models are adjusted for age, sex, etc. – even the crude model or just Model 1? Please clarify this in the legend of the table as well as in the Methods section.

Re: Sorry to make the reviewer confused. Here are detailed explanations: Model 1 was the crude model (unadjusted). Model 2 was adjusted for age, sex, education, annual household

income, smoking status, drinking and diabetes duration. Model 3 was additionally adjusted for remaining physical activity and sedentary time as appropriate. Model 4 was further adjusted for sleep duration. For models of 2 to 4, all subcomponents except zMS and waist circumference were additionally adjusted for waist circumference. When the dependent variable was fasting plasma glucose, we additionally adjusted for the use of glucose-lowering medication. For triacylglycerol and HDL-cholesterol we adjusted for the diagnosis of dyslipidemia and use of lipid-lowering medication. When the outcome of interest was systolic blood pressure, we additionally adjusted for the diagnosis of hypertension and use of antihypertensive medication. For the zMS we adjusted for the use of medication (glucose-lowering, lipid-lowering, and antihypertensive) and the diagnosis of dyslipidemia and hypertension. Details of relevant contents have been added in the legend of Table 3 (please see Page 27and 28), Table S3 and Table S4 as well as in the Methods section (please see Page 9, Paragraph 1).

Q17. - I suggest the authors eliminate the Table S3 from the manuscript. PA, sitting, and sleeping are behaviors that exclude each other, therefore, a low correlation between this variables are to be expected.

Re: Thank you for your suggestion. The Table S3 has been eliminated from our revised manuscript.

4. Discussion

Q18. - Please expand a little further on the potential implications of the results that ST and glucose correlate significantly in this study. Which possible biological mechanism could be responsible for the results? (Ceriello et al., 2000; Heine et al. 2004)

* Ceriello A. The post-prandial state and cardiovascular disease: relevance to diabetes mellitus.Diabetes Metab Res Rev. 2000; 16:125–132.

Heine RJ, Balkau B, Ceriello A, Del Prato S, Horton ES, Taskinen MR. What does postprandial hyperglycaemia mean?Diabet Med. 2004; 21:208–213.

Re: Thank you for your advice. The potential mechanism between sedentary time and fasting plasma glucose indicating involvement of markers of inflammation, insulin resistance, and adiposity. Obesity is associated with an increased risk of developing insulin resistance, may result in disordered regulation of glucose levels by reducing insulin release. The possible biological mechanism was discussed in Page 16.

Page 16, paragraph 2:-“The potential mechanism between sedentary time and fasting plasma glucose includes involvement of markers of inflammation, insulin resistance, and adiposity.

Obesity has been proved associated with increased risk of developing insulin resistance, and may result in disordered regulation of glucose levels by reducing insulin release."

Q19. - Sedentary behavior and physical activity patterns have been shown to vary between weekends and weekdays, because weekday ST activities and PA are likely to be more routine than at weekends. This would be relevant to discuss in regard of future studies.

Re: Thank you for your suggestion. We collected physical activity information through the Global Physical Activity Questionnaire. The self-reported measures of physical activity are known to have a relative low validity when compared to objective measures, in addition, physical activity and sitting data were not collected for weekends and weekdays respectively. This limitation have been discussed in Page 18.

Page 18, paragraph 1:-"Moreover, the patterns of physical activity and sedentary behaviors may vary between weekdays and weekends, but such variation is hard to be obtain by self-report measures used in the study. Further researches are needed to explore more detailed relationship between different pattern of physical activity and sedentary behavior (specifically comparing weekdays and weekends) with metabolic risks in type 2 diabetic patients."

Q20. - Results of a recent study suggest that there is limited evidence linking sitting and incident diabetes over 13 years (adjusted for moderate-to-vigorous physical activity and BMI) (Stamatakis et al., 2017). Therefore, please expand the discussion section on the potential impact of your study results. * Stamatakis E, Pulsford RM, Brunner EJ, et al. Sitting behaviour is not associated with incident diabetes over 13 years: the Whitehall II cohort study. Br J Sports Med 2017;51:818-823.

Re: Thank you for your suggestion. We have read this study carefully, Stamatakis et al. found that the association between sitting behavior and incident diabetes was attenuated when adjusted for BMI. Our findings suggested that more sedentary time was associated with higher waist circumference. We have discussed the potential mechanism and mentioned the limitation in Page 15-16.

Page 15 (paragraph 2), Page 16 (paragraph 1):- "However, the biological mechanisms for associations between sedentary time and waist circumference with metabolic risk are not fully understood yet. Results of a study reported that the association could be attenuated once adiposity component was included in the regression model. Our findings suggested that more sedentary time was associated with higher waist circumference, however, whether central obesity is a cause or a consequence of a sedentary behavior has not yet been fully elucidated. Sedentary time may displace physical activity time, leading to a decrease in energy expenditure and unfavorable weight changes. Additional pathways linking sedentary

time, waist circumference and metabolic risk include the established associations between major sedentary behavior (TV viewing) and unhealthy diet."

5. Conclusion

Q21. - I suggest the authors eliminate "lack of" and "excess" from the following sentence: "Our results suggest that lack of physical activity and excess sedentary time are both independently associated with clustered and individual metabolic risk in community type 2 diabetic patients."

Re: We have deleted the words "lack of" and "excess" in our manuscript according to your suggestion.

6. Discretionary Revisions

Q22. - The manuscript requires professional English editing.

Re: Thanks for your suggestions. In this revision, we invited a skilled English researcher to help polishing the English writings. We hope the revised manuscript is acceptable for you.

VERSION 2 – REVIEW

REVIEWER	Antje Ullrich University Medicine Greifswald Institute of Social Medicine and Prevention Walther-Rathenau-Str. 48 D-17475 Greifswald Germany
REVIEW RETURNED	22-May-2019

GENERAL COMMENTS	„Physical activity, sedentary time and their associations with clustered metabolic risk among people with type 2 diabetes in Jiangsu Province: A cross-sectional study. " Thank you to the authors for attending to my concerns in a detailed manner. The manuscript revisions have largely addressed my key concerns and the revisions have significantly improved the readability of the manuscript, with the exception of a few minor issues that are addressed below: Abstract • Please use instead of the term subjects the term individuals or participants in the participants section.

	• Please state the results of commuting physical activity in the conclusions section as well. • The conclusions section needs to be much stronger; in the sense that what are the consequences/ implications for practice or policy. Introduction • Please revise the section of the definition of sedentary behavior: “is any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalent task (MET) in a sitting or reclining posture.” • I suggest moving the sentence “While most attention has been focused…” [line 33; page 4] at the bottom of page 4 and inserting it before the sentence “Therefore, it is interesting to explore…”. • There are a growing number of studies that have examined joint associations between physical activity and sitting time and cardiometabolic factors or risk scores. Therefore, a directional hypothesis might state at the end of the introduction. This would also have consequences on uses statistical methods to check the validity of the hypothesis (one-sided versus two-sided statistical tests). Methods • I suggest the authors eliminate the sentence “The MET is a ration…” [line 17; page 6]. • It is stated that “Model 3 was additionally adjusted for remaining physical activity and sedentary time as appropriate;”. Do I understand correctly that the term "remaining physical activity" means that each individual domain of physical activity in model 3 has been adjusted for the other physical activity domains if appropriate? Please clarify this sentence. Results • Please present the percentage of women instead of those of men in your study. This is also in line with the information presented in the abstract section. • I propose to the authors to state the coefficient of determination (R2) of each regression model, because it is the proportion of variance in the dependent variable that is explained or predicted by the independent variable and is therefore a basis for making decisions about the practical importance of these factors. • Please revise the title of the Table S4; use instead of “…with metabolic variables”, “…with metabolic risk”. • In the revised version of the manuscript, I found no revised Figure 1. Thus, I cannot review this part of the manuscript. Discussion • The authors discussed their findings on the association between occupational physical activity and cardiometabolic risk. Further, they stated “This findings suggested a special importance of occupational physical activity as a single domain for the management of metabolic risk…”. The question remains whether and to what extent individuals have the opportunity to change physical activity within the occupation domain. It seems easier for the individual to change physical activity in commuting or leisure-time domain compared to the occupation domain. • The discussion on the association of commuting physical activity and cardiometabolic risk remains unclear. The discussion needs further explanations. One reason for the results may be the specific characteristics of the sample in this study.

	Conclusion • I suggest the authors eliminate “and longitudinal” from the following sentence “Findings from this study extend previous…”. Discretionary Revisions • The authors further use the term type 2 diabetic patients. Please revise carefully the whole manuscript. • In some parts, the authors used "sedentary behavior" and sometimes "sedentary behaviour." Please unify the language used (British versus American English). • The manuscript still requires professional English editing.

VERSION 2 – AUTHOR RESPONSE

Reviewer' comments and point-to-point responses:

Reviewer #1: Thank you to the authors for attending to my concerns in a detailed manner. The manuscript revisions have largely addressed my key concerns and the revisions have significantly improved the readability of the manuscript, with the exception of a few minor issues that are addressed below:

1. Abstract

Q1- Please use instead of the term subjects the term individuals or participants in the participants section.

Re: Thank you for your advice. We have changed the manuscript as suggestions (please see Page 2).

Page 2, Abstract:-“20,340 participants selected using stratified cluster-randomised sampling and an interviewer-managed questionnaire.”

Q2- Please state the results of commuting physical activity in the conclusions section as well.

Re: Thanks for your reminding. The results of commuting physical activity have been stated in the conclusion section (please see Page 2).

Page 2, Abstract:-“Commuting physical activity was inversely associated with triacylglycerol.”

Q3- The conclusions section needs to be much stronger; in the sense that what are the consequences/ implications for practice or policy.

Re: Thank you for your suggestion. The related context have been added in revised manuscript (please see Page 2).

Page 2, Abstract:-“These findings suggest that increased physical activity in different domains and decreased sedentary time may have a protective effect against metabolic risk in type 2 diabetes patients.”

2. Introduction

Q4-Please revise the section of the definition of sedentary behavior: “is any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalent task (MET) in a sitting or reclining posture.”

Re: Thank you for your advice. The definition of sedentary behavior have been revised in revised manuscript (please see Page 5)

Page 5, paragraph 2:-“Sedentary behaviours have been defined as any waking behaviour that is in a sitting, reclining, or lying down posture, expending little energy (i.e. 1.0 to 1.5 metabolic equivalents).”

Q5-I suggest moving the sentence “While most attention has been focused…” [line 33; page 4] at the bottom of page 4 and inserting it before the sentence “Therefore, it is interesting to explore…”.

Re: Thank you for your suggestion. We have removed the sentence at bottom of page 4 and inserted it before the sentence“Therefore, it is interesting to explore…” (Please see Page 5)

Page 5, paragraph 3:-“Furthermore, it has been suggested that using the continuous summary score of clustered metabolic risk (zMS) for analyses may improve the statistical power to detect associations, compared to using a binary definition of dichotomising continuous outcome variables. Many studies have focused on the risk of metabolic syndrome in Western populations, but the relationship between physical activity and sedentary time with the risk of metabolic syndrome is not well understood among Chinese populations. Although there have been a few studies in diabetic populations, their findings were inconsistent and limited by small sample sizes.”

Q6-There are a growing number of studies that have examined joint associations between physical activity and sitting time and cardiometabolic factors or risk scores. Therefore, a directional hypothesis might state at the end of the introduction. This would also have consequences on uses statistical methods to check the validity of the hypothesis (one-sided versus two-sided statistical tests).

Re: Thank you for your suggestion. A directional hypothesis have been stated at the end of the introduction (please see Page 6).

Page 6, paragraph 2:-“We hypothesised that physical activity is inversely associated with clustered and individual metabolic risk factors, whereas sedentary time increases such risk.”

2. Methods

Q7-I suggest the authors eliminate the sentence “The MET is a ration…” [line 17; page 6].

Re: Re: Your suggestion has been adapted and the sentence of “The MET is a ” had been deleted from this sentence.

Q8-It is stated that “Model 3 was additionally adjusted for remaining physical activity and sedentary time as appropriate;”. Do I understand correctly that the term

"remaining physical activity" means that each individual domain of physical activity in model 3 has been adjusted for the other physical activity domains if appropriate? Please clarify this sentence.

Re: I'm sorry that we did not explain it clearly. The term "remaining physical activity" means that each individual domain of physical activity in model 3 has been adjusted for the other physical activity domains if appropriate (please see Page 10).

Page 10, paragraph 1:- “ Model 3 was additionally adjusted for remaining physical activity and sedentary time, for each individual domain of physical activity was adjusted for the other physical activity domains and sedentary time as appropriate;”

3. Results

Q9- Please present the percentage of women instead of those of men in your study. This is also in line with the information presented in the abstract section.

Re: Thank you to point this out. We have presented the percentage of women in revised manuscript (please see Page 11).

Page 11, paragraph 4:-“Of the 17,750 participants included in the analyses, 60.3% were women.”

Q10- I propose to the authors to state the coefficient of determination (R2) of each regression model, because it is the proportion of variance in the dependent variable that is explained or

predicted by the independent variable and is therefore a basis for making decisions about the practical importance of these factors.

Re: Thank you for your advice. We have stated the coefficient of determination (R^2) of each regression model, the results are below:

Table 3 Cross-sectional linear regression analysis of association of physical activity and sedentary time with metabolic variables

	Physical activity (per-SD) ‡									
Metabolic risk	Total	R^2¶	Occupational	R^2¶	Commuting	R^2¶	Leisure-time	R^2¶	Sedentary time (per-SD) ‡	R^2¶
zMS†										
Model 1	-0.147(-0.187, -0.108)***	0.003	-0.132(-0.171,-0.093)***	0.003	-0.047(-0.086,-0.007)*	0.001	-0.068(-0.107,-0.029)**	0.001	0.188(0.148, 0.227)***	0.005
Model 2	-0.091(-0.126, -0.057)***	0.271	-0.077(-0.111,-0.042)***	0.271	-0.013(-0.047, 0.021)	0.282	-0.044(-0.078,-0.010)*	0.281	0.128(0.094, 0.162)***	0.282
Model 3	-0.080(-0.115, -0.046)***	0.274	-0.066(-0.101,-0.031)***	0.274	-0.011(-0.045, 0.022)	0.284	-0.042(-0.076,-0.008)*	0.283	0.121(0.087, 0.155)***	0.284
Model 4	-0.080(-0.114, -0.046)***	0.274	-0.066(-0.101,-0.031)***	0.274	-0.011(-0.045, 0.023)	0.284	-0.041(-0.075,-0.007)*	0.284	0.117(0.083, 0.151)***	0.284
Waist circumference (cm)										
Model 1	-0.552(-0.692, -0.412)***	0.003	-0.625(-0.765,-0.485)***	0.004	0.096(-0.044, 0.237)	0.001	-0.026(-0.167, 0.114)	0.001	0.575(0.435, 0.715)***	0.004
Model 2	-0.495(-0.635, -0.355)***	0.027	-0.519(-0.661,-0.376)***	0.028	0.021(-0.118, 0.161)	0.028	-0.051(-0.191, 0.089)	0.028	0.525(0.386, 0.663)***	0.028
Model 3	-0.450(-0.591, -0.309)***	0.030	-0.475(-0.618,-0.332)***	0.030	0.028(-0.112, 0.167)	0.030	-0.042(-0.182, 0.098)	0.030	0.483(0.344, 0.623)***	0.030
Model 4	-0.449(-0.591, -0.308)***	0.030	-0.475(-0.620,-0.334)***	0.030	0.030(-0.109, 0.170)	0.030	-0.039(-0.179, 0.102)	0.030	0.474(0.334, 0.613)***	0.030
Fasting plasma glucose(mmol/L) §										
Model 1	0.005(0.000, 0.010)	0.001	0.007(0.002, 0.012)**	0.001	-0.005(-0.010, 0.000)	0.001	-0.001(-0.006, 0.004)	0.001	0.011(0.006, 0.016)***	0.001
Model 2	0.003(-0.002, 0.007)	0.131	0.005(-0.001, 0.009)	0.131	-0.001(-0.005, 0.004)	0.131	-0.002(-0.007, 0.002)	0.131	0.008(0.004, 0.013)***	0.131
Model 3	0.004(-0.001, 0.008)	0.131	0.005(-0.001, 0.010)	0.131	-0.001(-0.005, 0.004)	0.131	-0.002(-0.007, 0.003)	0.131	0.009(0.004, 0.013)***	0.131

Model 4	0.004(-0.001, 0.008)	0.132	0.005(-0.001, 0.009)	0.133	-0.001(-0.005, 0.004)	0.133	-0.002(-0.006, 0.003)	0.133	0.008(0.003, 0.013)***	0.132
Triacylglycerol (mmol/L) §										
Model 1	-0.022(-0.030, -0.013)***	0.001	-0.017(-0.025,-0.009)**	0.001	-0.015(-0.024,-0.007)***	0.001	-0.020(-0.019,-0.003)**	0.001	0.031(0.023, 0.039)***	0.003
Model 2	-0.014(-0.021, -0.007)***	0.347	-0.009(-0.015,-0.002)*	0.348	-0.012(-0.019,-0.005)***	0.348	-0.007(-0.014,-0.001)*	0.348	0.017(0.010, 0.024)***	0.348
Model 3	-0.012(-0.019, -0.006)***	0.348	-0.007(-0.014,-0.001)*	0.348	-0.012(-0.019,-0.005)***	0.348	-0.006(-0.013, 0.001)	0.348	0.016(0.009, 0.023)***	0.348
Model 4	-0.012(-0.019, -0.006)***	0.348	-0.007(-0.014,-0.001)*	0.349	-0.012(-0.019,-0.005)***	0.349	-0.006(-0.013, 0.001)	0.349	0.015(0.008, 0.022)***	0.348
HDL-cholesterol (mmol/L)										
Model 1	0.015(0.009, 0.022)***	0.001	0.016(0.009, 0.022)**	0.001	0.002(-0.005, 0.008)	0.001	0.003(-0.004, 0.009)	0.001	-0.019(-0.025, -0.012)***	0.002
Model 2	0.010(0.004, 0.016)***	0.136	0.007(0.001, 0.013)*	0.136	0.003(-0.003, 0.009)	0.136	0.007(-0.001, 0.013)	0.136	-0.008(-0.014, -0.002)*	0.135
Model 3	0.009(0.003, 0.015)***	0.136	0.006(0.001, 0.013)*	0.136	0.003(-0.003, 0.009)	0.136	0.007(-0.001, 0.013)	0.136	-0.007(-0.013, -0.001)*	0.136
Model 4	0.009(0.003, 0.015)***	0.136	0.006(0.001, 0.013)*	0.136	0.003(-0.003, 0.009)	0.136	0.007(-0.001, 0.013)	0.136	-0.007(-0.013, -0.001)*	0.136
Systolic blood pressure (mmHg)										
Model 1	-0.907(-1.209, -0.604)***	0.002	-0.625(-0.928, -0.322)***	0.001	-0.549(-0.852,-0.246)***	0.001	-0.871(-1.174,-0.568)***	0.002	0.340(0.037, 0.643)*	0.001
Model 2	-0.110(-0.359, 0.139)	0.353	0.065(-0.187, 0.317)	0.354	-0.212(-0.459, 0.034)	0.354	-0.300(-0.548,-0.052)*	0.354	0.224(-0.022, 0.470)	0.353
Model 3	-0.091(-0.341, 0.159)	0.353	0.084(-0.169, 0.337)	0.354	-0.210(-0.456, 0.037)	0.354	-0.296(-0.544,-0.048)*	0.354	0.216(-0.031, 0.462)	0.353
Model 4	-0.096(-0.346, 0.155)	0.354	0.081(-0.173, 0.334)	0.354	-0.219(-0.466, 0.028)	0.354	-0.293(-0.542,-0.045)*	0.354	0.215(-0.033, 0.462)	0.354

Regression results are presented as unstandardized coefficients (B) (95%CI)

† zMS is a continuously distribute variable for clustered metabolic risk calculated by summing sex-specific standardized values for waist circumference, fasting plasma glucose, triacylglycerol, systolic blood pressure and the inverse of HDL-cholesterol.

‡ Per-SD of physical activity =13.8 MET-h/d, Per-SD of occupational physical activity =12.6 MET-h/d, per-SD of commuting physical activity =3.2 MET-h/d, per-SD of leisure-time physical activity=3.4 MET-h/d, per-SD sedentary time = 2.5 h/d

All models (except model 1) are adjusted for age, sex, education, annual household income, smoking status, drinking and diabetes duration. All outcomes except zMS and waist circumference are additionally adjusted for waist circumference. Fasting plasma glucose is additional adjusted for the use of glucose-lowering medication (yes/no); Triacylglycerol and HDL-cholesterol are additionally adjusted for the diagnosis of dyslipidemia (yes/no) and the use of lipid-lowing drugs (yes/no/unclear); Systolic blood pressure is additionally adjusted for the diagnosis of hypertension(yes/no) and the use of antihypertension medication (yes/no/unclear); and zMS is additional adjusted for the use of glucose-lowering medication (yes/no), lipid-lowing medication (yes/no/unclear) and antihypertension medication (yes/no/unclear), the diagnosis of dyslipidemia (yes/no) and the diagnosis of hypertension(yes/no).

Model 3 is adjusted for remaining physical activity and sedentary time as appropriate; Model 4 is additional adjusted for sleep duration

§ Fasting plasma glucose and triacylglycerol were logarithmically transformed (base e) due to their skewed distribution.

¶ R^2: Coefficient of determination.

Because the main purpose of our research was to adjust the confounding factors to explore the relationship between physical activity and sedentary behavior with metabolic risk, not to fit the model. The results of R-Squared values of each regression model were not included in our revised manuscript.

In addition, the R-Squared values of each regression model in our study of around 0.10 to 0.40, but R-squared does not indicate whether a regression model is adequate. You can have a low R-squared value for a good model, or a high R-squared value for a model that does not fit the data. Furthermore, if your R-squared value is low but you have statistically significant predictors, you can still draw important conclusions about how changes in the predictor values are associated with changes in the response value.

Q11- Please revise the title of the Table S4; use instead of "…with metabolic variables", "…with metabolic risk".

Re: Thank you for your reminding. We have revised the title of Table S4.

Q12- In the revised version of the manuscript, I found no revised Figure 1. Thus, I cannot review this part of the manuscript.

Re: Sorry to make the reviewer confused. The Figure 1 is below:

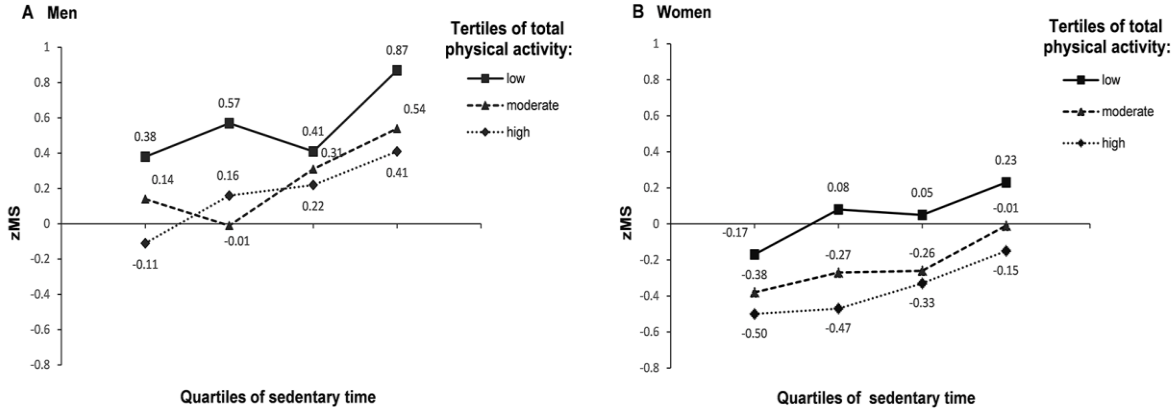

Fig 1. Means of clustered metabolic risk scores by sedentary time and physical activity among 17,750 diabetic patients. The adjusted mean was calculated using general linear regression models after adjustment for age. For physical activity, in men, the cut-off values for defining low, moderate, and high tertile groups were 4.00 and 11.14 MET-h/d, while they were 4.57 and 12.00 MET-h/d for women. For sedentary time, the 4 groups by quartiles of sedentary time were ＜2.2, 2.3-3.3, 3.4-4.9, and ≥5.0 h/d for men and ＜2.2, 2.3-3.3, 3.4-4.4, and ≥4.5 h/d for women. MET, metabolic equivalent task.

4. Discussion

Q13- The authors discussed their findings on the association between occupational physical activity and cardiometabolic risk. Further, they stated "This findings suggested a special importance of occupational physical activity as a single domain for the management of metabolic risk…". The question remains whether and to what extent individuals have the opportunity to change physical

activity within the occupation domain. It seems easier for the individual to change physical activity in commuting or leisure-time domain compared to the occupation domain.

Re: Thank you for your advice. In our study, occupational physical activity including farm work, housework and factory work (Please see Table S1). There are 75.8% of patients were famers, homemakers and retirees (data are not shown in our manuscript). Furthermore, about 22.4% are famers and 33.0% are homemakers who do not have fixed retirement time, and more than half of retirees also engaged in housework after retirement. So it is feasible for individual to change physical activity in occupation domain.

Q14- The discussion on the association of commuting physical activity and cardiometabolic risk remains unclear. The discussion needs further explanations. One reason for the results may be the specific characteristics of the sample in this study.

Re: Thank you for your suggestion. The detailed context have added in revised manuscript (please see Page 15).

Page 15:-“In a recent study, a trend was observed between lower levels of commuting physical activity and higher metabolic risk. Our findings have also suggested that commuting physical activity is inversely associated with triacylglycerol, but there was no statistically significant association observed between commuting physical activity and clustered metabolic risk in this study, similar to the finding of the J-ECOH study. This may partly be explained by the low level of commuting physical activity in our study, since 40% of patients reported that they did not engage in commuting physical activity.”

5. Conclusion

Q15- I suggest the authors eliminate “and longitudinal” from the following sentence “Findings from this study extend previous…”.

Re: We have deleted the words “and longitudinal” in revised manuscript according to your suggestion.

6. Discretionary Revisions

Q16-The authors further use the term type 2 diabetic patients. Please revise carefully the whole manuscript.

Re: Thank you very much for the comments, we have checked the whole manuscript and revised accordingly.

Q17- In some parts, the authors used "sedentary behavior" and sometimes "sedentary behaviour." Please unify the language used (British versus American English).

Re: Thanks for your reminding. We have used " behaviour" in the whole manuscript

Q18- The manuscript still requires professional English editing.

Re: Thanks for your suggestions. This manuscript was edited for English language by

Editage (www.editage.cn).

VERSION 3 - REVIEW

REVIEWER	Antje Ullrich University Medicine Greifswald Institute of Social Medicine and Prevention Greifswald, Germany
REVIEW RETURNED	03-Jul-2019

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.