Author's response to reviews

Title: Long working hours and metabolic syndrome among Japanese men: a cross-sectional study

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Author's response to reviews:

Profession Natalie Pafitis
Editor-in-Chief, BMC Public Health
Professor Ludovic van Amelsvoort
Associate Editor, BMC Public Health

16 April, 2012

Dear Professor Pafitis and Professor van Amelsvoort,

We are sending herewith a revised manuscript entitled “Long working hours and metabolic syndrome among Japanese men” (9730148236710012) by T Kobayashi, et al. which we would like to submit for the publication in BMC Public Health as a research article.

Following the reviewers’ comments, we carefully revised our manuscript. We are grateful to hear the positive evaluation of our article by the Editor. Following the Editor’s comment, we added citations to some important papers, related on the topic. With regard to the use of English language, please note that our manuscript had been already edited by a professional editing service (Edanz) before we submitted the original version to the Journal. Given the thorough revision, however, we decided to send our manuscript to a professional editing service (Edanz) again so that the use of English language is revised and improved to make our manuscript more readable for the general readers.

We take public responsibility for its validity and final presentation as an original publication. We declare that there are no conflicts of interest. We state here that this is an original work, which has not been published in any journals, either in whole or in part, or is not under review elsewhere.

We thank all the reviewers again for their helpful comments, which we feel have improved our manuscript. We hope that with these modifications, our paper can now be accepted for publication in BMC Public Health.
Your sincerely,
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Responses to Reviewers’ comments (9730148236710012)
Reviewer 1
Dear Dr. Karlsson:

Thank you very much for your thoughtful review and positive evaluation of our article. We have revised our manuscript in response to your suggestions. Our responses are described in normal font following the reviewer’s comments in boldface.

Minor revision:

1. Methods: The number of individuals with unavailability to electronic data of health checkup are rather high. Is there a possible social bias due to that, beyond what is described on page 10?

Response:

In accordance with your comment, we thoroughly examined differences between analyzed and unanalyzed participants. Although there was no significant difference in occupation, there were significant differences in age, working hours, sleeping hours, and cohabiting status. As a possibility of social bias cannot be fully excluded, the revised manuscript thoroughly explains these differences. We hope that this information would be helpful to readers to understand the possible social bias. Since we had already explained the significant differences in age, working hours, and sleeping hours in the original version, we added sentences to explain the significant difference in cohabiting status as follows:

(Page 12 line 7)

Although there was no significant difference in occupation, there was a significant difference in cohabiting status; 344 (91.0%) unanalyzed subjects cohabited whereas 731 (78.4%) analyzed subjects cohabited.

2. Results: Why is the dichotomized level of 40 years chosen? Has other levels been tested?

Response:

We chose the dichotomized level of 40 years following the Act on Assurance of
Medical Care for Elderly People in Japan, which focused on metabolic syndrome among people aged 40–74 years. When we stratified the subjects by using other cut-off values (e.g., 45 years and 50 years), similar patterns were observed, and we decided to show them by using Supplementary Tables 2 and 3. In accordance with your suggestion, we added sentences as follows:

(Page 9 line 6)
Furthermore, we conducted a stratified analysis by age (<40 years vs. ≥40 years) following the Act on Assurance of Medical Care for Elderly People in Japan [23], which focused on metabolic syndrome among people aged 40–74 years.

(Page 11 line 6)
Similar patterns were observed when we stratified the subjects using other cut-off values (e.g., 45 years and 50 years, as shown, respectively, in Supplementary Tables 2 and 3).

3. Discussion and conclusions: In general are the findings very discussed in reference with the existing scientific literature. About intervention strategies discussed on page 16. Japan is known for “existing long working hours” in the labour market. Simultaneously, the law is restrictive. How is it possible to combine that fact with the actual demands of the Labor Standards Law (40h/w)? In other words, it would be of interest from an European point of view to better understand the proposal about not to use a high risk strategy intervention, than population strategy intervention.

Response:
Thank you very much for your thoughtful comment. The Labour Standards Law regulates prescribed working hours within 40 hours/week in Japan. However, in addition to prescribed working hours, an employer can extend working hours for 45 hours/month beyond the Law limits; when it is clarified why workers are required to work overtime, an employer makes an agreement about the extension of working hours. In accordance with your suggestion, we clarified our conclusions as follows:

(Page 19 line 14)
Though significant efforts are needed to manage the individual abnormalities of metabolic syndrome and the prevention of metabolic syndrome is essential in reducing cardiovascular disease [2], the findings of the present study may indicate the necessity of a well-designed population strategy for metabolic syndrome [57], given the existing culture of long working hours in Japan. Despite the working-hour regulations specified by the current Labour Standards Law, there is an exceptional rule whereby an employer can extend the working hours by an additional 45 hours/month. Further studies are required to examine whether proper management of working hours can serve as a primary preventive measure for metabolic syndrome.

Reviewer 2
Dear Dr. Bøggild:

Thank you very much for your thoughtful review and positive evaluation of our article. We have revised our article following your helpful comment. Our response is described in normal font following the reviewer’s comment in boldface.

Major Compulsory Revisions

1. Measures are partly described at p.7. I miss a description of how measures of waist circumference, triglycerides, HDL, treatment for hypercholesterolemia or hypertension and blood pressure were conducted, and whether health check-up was conducted in any specific time of the day. Having triglycerides, HDL and blood pressure measured could be influenced by strain, by having eaten just before the examination, by having rushed to work etc.

Response:

We apologize that we did not provide a detailed description of measures. Health checkups were conducted in the morning of a day specified by the company during working hours; to obtain accurate measures, they were also required to observe an overnight fast. Also, blood pressure measurement is usually arranged in late among prescribed exam items and is remeasured if the measurement is likely to be influenced by strain of work. As we could not obtain information about treatment for hypercholesterolemia or hypertension from health checkups, we applied Japanese criteria except for current medication use. In line with this, we revised description of current medication use in the Methods section and added this point as a limitation in the Discussion section. In accordance with your suggestion, we added sentences as follows:

(Page 7 line 7)

We applied the Japanese criteria for metabolic syndrome [23] except with respect to medication, details of which were not available in the present study. Thus, metabolic syndrome was defined as having a waist circumference of #85 cm and at least two of the following three conditions: (1) high serum triglyceride (#150 mg/dl) and/or low high-density lipoprotein (HDL) cholesterol (<40 mg/l); (2) high blood pressure (#130/85 mmHg); and (3) high fasting plasma glucose (#110 mg/dl). Waist circumference was measured at the umbilical level using non-elastic tape by a medical staff member. Serum triglyceride, HDL, and fasting plasma glucose were measured with fasting blood specimens using, respectively, a glycerol removal method, an enzymatic method, and a stepwise high-performance liquid chromatography method. Blood pressure was measured with the subject in a sitting position by means of a sphygmomanometer on the arm. Each subject was required to undergo a health checkup in the morning of a day specified by the company; to obtain accurate measures, they were also required to observe an overnight fast (no food after 9 p.m.).

(Page 18 line 16)

Third, owing to lack of information about the use of medication, the possibility of misclassification of diseased as non-diseased conditions cannot be ruled out.
This misclassification, however, would be non-differential, which may have attenuated the present results.

2. Several categories in occupational status (“sales”, “others” and “missing”), shift work, alcohol consumption and cohabiting (table 1) have very low numbers; how was this handled in the modeling (table 2, model 3), were they excluded?

Response:
We treated categorical variables as dummy variables, including occupation (“sales” and “others”), shift work, frequency of alcohol consumption, and cohabiting status. Further, we excluded subjects with “missing” values from the analysis. In accordance with your comment, we added a sentence as follows:

(Page 8 line 17)
Categorical variables were included as dummy variables, and subjects with missing values were excluded from the analysis.

3. Are the sociodemographic factors presented in the paper associated with metabolic syndrome in the sample and/or in the literature? Could any of them be left out in the final model in order to have more robust estimates? This should be expanded.

Response:
We selected the covariates in Model 3 in reference to past studies. In accordance with your suggestion, we modified the sentence and added citations to explain the association between each sociodemographic factor and metabolic syndrome as follows:

(Page 8 line 15)
In Model 3, we additionally adjusted for the following variables with reference to previous studies: occupation [24], shift work [25], smoking status [26, 27], frequency of alcohol consumption [28], and cohabiting status [29].

4. In table 1 sleeping seems to be heavily associated with working hours, but it doesn’t seem to be further investigated in the models. Why is this?

Response:
As has been noted, sleeping hours can be a mediator of the association between long working hours and metabolic syndrome. Thus, we decided not to adjust for sleeping hours in Model 3. To clarify this, we added a sentence as follows:

(Page 9 line 1)
We did not adjust for sleeping hours in Model 3 since sleeping hours were treated as a mediator of the association between long working hours and metabolic syndrome [30].

Please note that Reviewer 3 suggested reporting what happens to the association before and after adjustment for sleeping hours to see whether short
sleep contributes to the association (see her comment No. 7). In response to this, we added a sentence as follows:

(Page 10 line 12)
When we additionally adjusted for sleeping hours (continuous) as a supplementary analysis, the positive association was slightly attenuated: the ORs for 8–9, 9–10, and >10 working hours/day were 1.61 (95% CI, 0.88–2.92), 1.36 (95% CI, 0.69–2.68), and 1.86 (95% CI, 0.82–4.22), respectively.

5. Especially occupational status “technicians” and “skilled” are respectively strongly associated and reversely associated with work hours (table 1). Also age seems to be inversely associated with working hours. How robust are the models - more information on this is needed. I find the restricted models very useful, could this be used further, restricting for instance to technicians or skilled workers alone?

Response:
In accordance with your suggestion, we further restricted the analysis to technicians or skilled workers and added sentences in the Methods, Results, and Discussion sections as follows:

(Page 9 line 9)
Finally, we restricted the analyses a posteriori to technicians or skilled workers to examine the possible effect of modification across occupations.

(Page 11 line 9)
Finally, we restricted the analysis to technicians or skilled workers. It should be noted that these two categories comprised the majority of the subjects. We observed heterogeneous results across the two types of occupation, although the precision of the estimates was considerably low. Among technicians, the multivariate ORs for 8–9, 9–10, and >10 working hours/day were 2.00 (95% CI, 0.38–10.57), 1.36 (95% CI, 0.27–6.78), and 1.86 (95% CI, 0.39–8.86), respectively. By contrast, among skilled workers, the multivariate ORs for 8–9 and 9–10 working hours/day were 1.66 (95% CI, 0.80–3.45) and 1.45 (95% CI, 0.56–3.71), respectively (the OR for >10 hours/day was not available owing to a lack of data).

(Page 17 line 15)
Interestingly, when we further examined the association between working hours and metabolic syndrome by restricting the analysis to technicians and skilled workers, we observed heterogeneous results with respect to occupation. Given the considerably low precision of the estimates, it is necessary to exercise caution when interpreting the results of this supplementary analysis. This finding may, however, indicate the significance of occupation when examining the association between working hours and metabolic syndrome. This point has been less carefully examined and, given the widening health disparities across occupations for both sexes during the recent economic downturns in Japan [52,
future studies are necessary to investigate this possible heterogeneous effect.

6. I find that the results are not as clear as stated in the paper. In model 2 (table 2) adjusting for age, shows that the highest ratio is seen for the 8–9 hours group, this point estimate is further raised in the final model 3, while the >10 hours group has a lower point estimate in model 2 and only just reaches statistical significance in model 3 (2.31 (1.04-5.14). The 9-10 hours group has a lower point estimate in both models, which is not commented on. The “benchmark” approach (p.11, l. 14) does not explain the pattern in the slightly elevates work hours group. Both in the restricted models (table 3, >40 year) and in the additional table the same pattern is seen with a modest elevated point estimate in the 9-10 hour group, a high ratio in the 8-9 hour group and estimate in the >10 hour a day group, that have the highest estimate only in the fully adjusted model. This should in my opinion be further investigated and commented on. I suspect that the final model could cover for spurious results.

Response:
Thank you for your thoughtful comment. In accordance with your suggestion, we modified sentences to describe the present findings more clearly as follows:

When we adjusted for health-related behavior (i.e., smoking status and frequency of alcohol consumption) in addition to age, the ORs did not change substantially. When we subsequently adjusted for shift work and cohabiting status, the ORs of the 8–9 working hours/day and >10 hours/day slightly increased. Finally, when we additionally adjusted for occupation, the positive association between working hours and metabolic syndrome was enhanced (Model 3); those who worked >10 hours/day had more than double the odds of metabolic syndrome (OR, 2.32; 95% CI, 1.04–5.16).

Indeed, the point estimates of ORs in Models 1 and 2 were the highest among those who worked 8–9 hours/day, and we observed a dip among those who worked 9–10 hours/day in Models 1 to 3. The increased ORs among those who worked 8–9 hours/day, however, could be partially explained by the effect of the Labour Standards Law, which stipulates that working hours be limited to 40 hours/week. Workers who developed health problems may have been required to restrict their working hours to avoid further adverse health outcomes arising from long working hours. This so-called healthy worker effect could also have been induced by self-regulation among subjects who have higher control over their work schedule, and this tendency may be more pronounced in workplaces with a higher social network or social capital [32-34].

7. As stated, this is a cross-sectional study, and the conclusions drawn, both in the abstracts and paper (p.16), is not covered by the results. It is not possible to infer whether a reduction in working hours lowers the “risk” of metabolic syndrome or to judge whether reductions are a feasible prevention strategy. I
would suggest rewriting the conclusion in order to downplay the implications of the study.

Response:
Thank you for your thoughtful comment. In accordance with your suggestion, we deleted the following sentences from the abstract and the Conclusions in the main text, and thoroughly revised them:

(Page 3 line 5 in the original version)
Although a variety of lifestyle factors could influence the risk of metabolic syndrome among the working population, the present findings may well lead to future interventions to promote health and to decrease the risk of metabolic syndrome, by adequate control of working hours.

(Page 16 line 4 in the original version)
Although a variety of lifestyle factors, including short sleeping time and diet, could influence the risk of metabolic syndrome among the working population, the present findings may well lead to future interventions to promote health and to decrease the risk of metabolic syndrome, by adequate control of working hours.

8. I find that the language needs a thorough revision.

Response:
Our manuscript had been already edited by a professional editing service before we submitted the original version to the Journal. (We submit a certificate to the Journal to indicate that language in our manuscript had been checked by a native-English-speaking scientist.) Given the thorough revision, however, we decided to send our manuscript to a professional editing service again so that the use of English language is revised and improved to make our manuscript more readable for the general readers.

Minor Essential Revisions
1. In the tables I suggest including the number of participants in the models.

Response:
In accordance with your suggestion, we added the number of participants in Tables 1 to 3 and Supplementary Tables 1 to 3.

Discretionary Revisions
1. The paper describes in sufficient detail how the original material came from 1664 invited workers to the 934 used. I would suggest, however, describing only the male population, from male workers to the 934 used. Instead the authors could explain in short that the female population was excluded due to lack of overtime. In line with this, the paragraph on “Characteristics of unanalyzed participants” (p. 10) should also not mention the women population.

Response:
In accordance with your suggestion, we modified the sentences in the Methods and deleted descriptions of women in the paragraph on “Characteristics of unanalyzed participants”:

(Page 6 line 5)
Almost all the subjects responded to the questionnaires before the health checkup: of the 1,664 study subjects, 1,601 returned the questionnaire, and the response rate was 96.2% (1,314 men, 287 women). We restricted the analysis to men since 78.8% of the women did not work overtime, which precluded further analysis between working hours and metabolic syndrome among women. Of the remaining 1,314 men, we excluded participants who did not respond to the questionnaire item on working hours (n=27), those who worked fewer than 7 hours/day (n=2), and those who for administrative reasons lacked annual health checkup information, e.g., unavailability of electronic data relating to the checkup (n=352). Thus, 933 men were included in the analysis.

2. I suggest using the term prevalence instead of risk (p.16, l.3: “…more than double the risk of metabolic…”), as the term “risk” implies a cause-and effect association, that can’t be justified despite the discussion on p. 15.

Response:
In accordance with your suggestion, we carefully avoided using the term “risk” in the above-mentioned context throughout the manuscript. When appropriate, to describe the findings more accurately, we decided to use the term “odds” as follows:

(Page 10 line 9)
Finally, when we additionally adjusted for occupation, the positive association between working hours and metabolic syndrome was enhanced (Model 3); those who worked >10 hours/day had more than double the odds of metabolic syndrome (OR, 2.32; 95% CI, 1.04–5.16).

(Page 12 line 13)
This study suggests that compared with subjects who work 7–8 hours/day, those reporting long working hours (>10 hours/day) had over double the odds of metabolic syndrome after adjusting for age, occupation, shift work, smoking status, frequency of alcohol consumption, and cohabiting status.

(Page 19 line 12)
We have found that compared with normal working hours (7–8 hours/day), long working hours (>10 hours/day) are associated with more than double the odds of metabolic syndrome among Japanese male workers.

3. What is meant by “average sleeping hours” (p.8, l. 1) - is it sleeping length?

Response:
We apologize for the lack of clarity. We measured sleeping length per day for the
past month on average. In accordance with your comment, we added a sentence as follows:

(Page 8 line 8)
Average sleeping hours were obtained using the following question: “How many hours did you sleep per day over the past month on average?”

4. In “Statistical analysis” (p.8) p-values are used to judge whether a value is statistical significant. The models are give 95% CI and not p-values, which I find very relevant. I would therefore suggest not to mention the p-values, rephrasing the sentence to “A confidence interval excluding 1 was considered statistical significant” or smoothing like that.

Response:
In accordance with your suggestion, we modified the sentence as follows:

(Page 9 line 11)
Odds ratios (ORs) and 95% confidence intervals (CIs) for metabolic syndrome were calculated, and a CI excluding 1 was considered statistically significant.

5. On p. 9, 2. Paragraph, l. 3: “…among workers with long working hours were all above null”, should probably read: “…above one”?

Response:
In accordance with your suggestion, we modified the sentence as follows:

(Page 10 line 5)
In Models 1 and 2, no statistically significant associations were observed, although the point estimates of ORs among workers with longer working hours were all above 1.

6. Table 1, p. 26, Sleeping. I suppose the (hours/day; mean; SD) line is the mean sleeping length, while the next three lines are the table. This could be made more explicit.

Response:
We apologize for the lack of clarity. In accordance with your suggestion, we decided to report only mean and standard deviation of sleeping hours in Table 1, which is also in line with the suggestion of the the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement No. 14.

Reviewer 3
Dear Dr. Virtanen:

Thank you very much for your thoughtful review and positive evaluation of our article. We have revised our manuscript in response to your suggestions. Our responses are described in normal font following the reviewer’s comments in
1. There is another study on working hours and metabolic syndrome: Violanti et al. Arch Env Occup Health 2009. However, in that study, metabolic syndrome was examined in a combination of shift working policeman and the study population was small.

Response:
Thank you for letting us know about this study. We added a citation to this study and modified the sentence as follows:

(page 5 line 6)
Although one study reported that overtime combined with midnight shift work may be a risk factor for metabolic syndrome, that study was based only on 98 police officers in the United States [21].


Response:
Thank you for your comment. We added citations to all papers you mentioned and modified the sentence as follows:

(page 4 line 14)
Previous studies have examined the effects of long working hours on various health outcomes, such as body mass index and waist circumference [7,8], obesity [9], hypertension [10-12], diabetes [13-15], acute myocardial infarction [16], and coronary heart disease [17-19].

3. Methods: Please provide some information on the distribution of working hours. How many employees worked part-time? Because part-time work is associated with serious health problems such as CHD it is preferable to either exclude them or treat them as a separate group (see e.g., Sokejima & Kagamimori, 1998)

Response:
We totally agree that we should exclude part-time worker or treat them separately. In reference to the study by Sokejima and Kagamimori (1998), we decided to exclude subjects who worked less than 7 hours/day (n=2). Thank you for your suggestion. We modified the sentences as follows:

(page 6 line 10)
Of the remaining 1,314 men, we excluded participants who did not respond to the questionnaire item on working hours (n=27), those who worked fewer than 7 hours/day (n=2), and those who for administrative reasons lacked annual health checkup information, e.g., unavailability of electronic data relating to the checkup
(n=352). Thus, 933 men were included in the analysis.

(Page 7 line 3)
We divided the participants into the following four categories of working hours: #7 to 8 hours/day, >8 to 9 hours/day, >9 to 10 hours/day, and >10 hours/day.

4. Do you have any information about participants’ CHD status? CHD can be a confounder which should be either adjusted or the cases excluded.

Response:
Unfortunately, information about CHD status was not available in this study. Thus, we adjusted for smoking status and frequency of alcohol consumption, which we think could be interpreted as proxy variables of CHD status. Although CHD status can be a confounder between working hours and metabolic syndrome, we also note that CHD status can be induced by metabolic syndrome, that is, metabolic syndrome mediates the association between working hours and CHD status. If this is the case, CHD status should not be adjusted for because adjustment for the effect of outcome could potentially yield a spurious association between exposure and outcome.

5. Do you have information on physical activity? If possible, that could be included as a covariate.

Response:
Unfortunately, information about physical activity was not available as we had already stated in the Study limitations of the Discussion section as follows:

(Page 19 line 3)
Fifth, information about physical activities and job stress was not available. Since these factors potentially mediate the association between working hours and metabolic syndrome, their assessment would promote our understanding of this cause-effect relationship [54-56].

6. Table 2: It seems that your association emerges in Model 3. Is it due to the adjustment for socioeconomic status or some of the other covariates? This additional analysis could be reported in the text.

Response:
The positive association between working hours and metabolic syndrome was enhanced when we adjusted for socioeconomic status (especially occupation). To clarify this, in accordance with your suggestion, we added sentences in the Results section as follows:

(Page 10 line 5)
When we adjusted for health-related behavior (i.e., smoking status and frequency of alcohol consumption) in addition to age, the ORs did not change substantially. When we subsequently adjusted for shift work and cohabiting status, the ORs of the 8–9 working hours/day and >10 hours/day slightly increased. Finally, when
we additionally adjusted for occupation, the positive association between working hours and metabolic syndrome was enhanced (Model 3); those who worked >10 hours/day had more than double the odds of metabolic syndrome (OR, 2.32; 95% CI, 1.04–5.16).

Additional information:

# ORs (8–9, 9–10, >10 hours/day) adjusted for age, smoking status and frequency of alcohol consumption: 1.58 (95% CI: 0.93–2.69), 1.40 (95% CI: 0.80–2.45), 1.55 (95% CI: 0.86–2.82), respectively.

# ORs (8–9, 9–10, >10 hours/day) adjusted for age, smoking status, frequency of alcohol consumption and cohabiting status: 1.51 (95% CI: 0.89–2.58), 1.22 (95% CI: 0.68–2.16), 1.47 (95% CI: 0.82–2.17), respectively.

# ORs (8–9, 9–10, >10 hours/day) adjusted for age, smoking status, frequency of alcohol consumption, cohabiting status and shift work: 1.61 (95% CI: 0.94–2.76), 1.31 (95% CI: 0.74–2.35), 1.71 (95% CI: 0.92–3.20), respectively.

7. Employees who work long work hours seem to have better health habits than those working shorter hours. You should report statistical tests for Table 1 (which associations were significant?). The only exception is sleeping hours, thus, can you show what happens to the association shown in Table 2 before and after adjustment for sleeping hours to see whether short sleep contributes to the association? If the association remarkably attenuated, then sleeping hours can be a mechanism explaining the association.

Response:

We agree that employees who work long work hours seem to have better health habits than those working shorter hours. We, however, decided not to report statistical tests in Table 1 following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement No. 14, which explains, “Inferential measures such as standard errors and confidence intervals should not be used to describe the variability of characteristics, and significance test should be avoided in descriptive table. Also, P values are not an appropriate criterion for selecting with confounders to adjust for in analysis.” With regard to adjustment for sleeping hours, we conducted further analysis following your suggestion and added sentences as follows:

(Page 10 line 12)

When we additionally adjusted for sleeping hours (continuous) as a supplementary analysis, the positive association was slightly attenuated: the ORs for 8–9, 9–10, and >10 working hours/day were 1.61 (95% CI, 0.88–2.92), 1.36 (95% CI, 0.69–2.68), and 1.86 (95% CI, 0.82–4.22), respectively.

(Page 15 line 10)

When we additionally adjusted for sleeping hours as a supplementary analysis, we observed a slight attenuation in the positive association between working hours and metabolic syndrome. Although careful consideration is required with its interpretation, this finding may support the above-mentioned hypothesis [44, 45].
8. Discussion: metabolic syndrome is close to type 2 diabetes. There are so far at least three studies on long working hours and type 2 diabetes with contradicting results (Kawakami et al., JECH 1999, Nakanishi et al. OEM 2001, Kronke et al. AJE 2007). You could reflect your findings in relation to these.

Response:
Thank you for your suggestion. We had already cited the paper by Kawakami et al. in the Discussion section to comparatively discuss the present findings. In accordance with your comment, we added citations to the papers by Nakanishi et al. and Kronke et al. and added sentences in the Discussion section as follows:

(Page 13 line 10)
A six-year study of women in the Nurses’ Health Study II indicated that subjects who worked #41 hours/week were associated with a higher risk of type 2 diabetes than those who worked 21–40 hours/week [14]. In contrast, Nakanishi et al. [15] reported that among Japanese male workers, the relative risk of type 2 diabetes significantly decreased among those who worked >10 hours/day compared with those who worked 7–8 hours/day.

We thank all the reviewers again for their helpful comments, which we feel have improved our manuscript. We hope that with these modifications, our paper can now be accepted for publication.

Sincerely,