PEER REVIEW HISTORY

This paper was submitted to the BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper went through the process of review and revision twice more at BMJ Open before it was accepted for publication.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Social and geographic inequalities in premature adult mortality in Japan: an observational study from 1970 to 2005
AUTHORS	Etsuji Suzuki, Saori Kashima, Ichiro Kawachi and S V Subramanian

REVIEW FROM THE BMJ

REVIEWER	Peter Goldblatt Deputy Director Institute of Health Equity Department of Epidemiology and Public Health University College London United Kingdom No competing interests

GENERAL COMMENTS	This paper is welcome in bringing together information on occupation and prefecture of residence from death registration at working ages across a 35 year period for the whole of Japan. Trend data presented on the change in occupational distribution and in patterns of mortality over this period are extremely valuable, as is the analysis of the inter-relationship between occupation, prefecture and social factors. However the findings are difficult to interpret and there are some key questions about the methods used and definitions which are not clear from the paper. These issues are explained in more detail below. Greater clarity about these issues is required before publishing what are on the face of it some extraordinary findings. Methods and definitions The social information in this study appears to derive from a comparison of major occupational groups as recorded at death and compared with Census denominators. There are two issues here. Fist occupational classifications, on their own do not equate to social classifications. To arrive at a social classification from an occupational classification requires two further steps. Firstly, identifying the status in employment of the individual - do they manage or supervise others in the occupational group. Secondly, the occupation and status combination needs to be graded according to the predominant type of employment contract for that combination (e.g. salaried, weekly wage, etc.). It does not appear that this has been carried out for the data used in the article. Clarification of this is essential - is this purely an occupation mortality

	analysis or is it an analysis according to social position? The second issue concerns the method of data collection. Is there any potential for numerator denominator bias between the two sources of information (census and death)? Specifically, what questions are asked on the two occasions and who are the respondents on the two occasions? In most cross-sectional occupational studies, discrepancies in either or both of these respects lead to numerator denominator bias. The extent of this is not clear from the paper. Nor is it clear from the paper whether any studies have been carried out in Japan to quantify any biases (either longitudinal follow up of census or retrospective in-depth surveys based on death records)f . Specific issues are whether, by the time a person dies they are either no longer in the occupation recorded for them at Census or whether the person recording the death either promotes the deceased to a higher status job or demotes them because they did not know the details of their job). As a simple example, it is not uncommon for those in lower status jobs to be selected out of the workforce due to ill health and be recorded as not employed or not classified at death, depending on the question asked at death. Mortality levels The odds ratios shown in Table 1 are startling. A four-fold difference in mortality for men classified to an occupation and a 16-fold difference for women. Furthermore, most of the substantial differences recorded are in the opposite direction to those seen in longitudinal data in the West. If true, this would imply a catastrophic loss of life in higher status social groups in Japan. However, although the paper looks at several possible explanations (stress, lifestyles, behaviours) it does not identify any biologically plausible explanation for this phenomenon. In terms of previous knowledge, is there a major threat to job security among the best-off in Japanese society? Do they suffer from effort-reward imbalance or a lack of control in their lives or jobs? No evidence or plausible hypothesis is proposed in the paper. Geographic differences The paper identifies some significant differences in mortality across Japan, with some interesting time trends. However, it does not present clear social and other correlations to help explain these patterns and trends. Part of the difficulty may be that, as the paper suggests, the prefectures are so large that they subsume as much within area social and mortality variation as exists between prefectures. If so, the observed patterns may simply be an illustration of the well-known ecological fallacy. A second problem may be that the paper, as noted above, has not identified a biologically plausible explanation for overall social inequalities in mortality. Without this modelling of the interaction between social factors, geography and mortality may be over-ambitious.

REVIEWER	Bjørn Heine Strand, researcher, Norwegian Institute of Public Health, Norway. I have no competing interests.

REVIEW RETURNED	28/11/2011

GENERAL COMMENTS	This is an interesting and well written piece of work extending the existing literature on social inequality mortality trends to also cover Japan. Previous studies on this topic have mainly focused on Western populations. This work is of importance to researchers and policymakers and might be well suited for a general medical journal like BMJ. Research questions are clearly defined. Furthermore, the design of the study is appropriate and by using multilevel methods they ensure to properly adjust for micro- macrolevel bias, as the author Subramanian earlier have described in his paper with Duncan and Jones (Environment and Planning A 2001, volume 33, pages 399-417). Nevertheless, I still miss some basic numbers; for example age adjusted mortality rates by occupational class by year and gender. Such numbers are modeled in Figure 1 and 2, but I suspect the linear trends might be too simplistic, and would like to get an idea of the background numbers before they are run through complicated models. I believe some readers of BMJ will find such multilevel models rather complicated. Data is census based and covers the whole of Japan so exclusion criteria are not highly relevant here. Participants are adequately described. The multilevel approach is a nice one as commented on above, but the choice of logit link function limits the results to the relative scale presented to the reader as odds ratios. The inequality literature has stressed the importance to also investigate absolute inequalities (se for example Oakes & Kaufman, Methods in social epidemiology, 2006). This is of special importance when looking at mortality trends as rates tend to decline over time and one can have the situation that all socioeconomic groups decrease their rate at similar pace, thus absolute differences are constant, but the relative rate will increase. Table 1 shows increasing ORs, but I suspect this fallacy just described could be the reason for this? Would it be possible to run the model using identity link and get RD? I have a concern regarding the revision of the classification of occupations and comparability of the 11 groups over time. For example, in group 9 “Production process and related workers” mining workers were included until 1986, but not in the last revision. I suspect mining workers have high mortality rate which could result in group 9 getting higher mortality in the earlier periods. Could this and other changes in the classification affect the results? I especially think of the pattern seen in Figure 1, where some groups, among them group 9, have a rather steep mortality decline. The pattern in men is somewhat strange as lines cross, putting high mortality occupational groups in 1970 among the lowest in 2005 (Sales workers). In women the picture is more harmonized, with decline in mortality in all groups (fig 2). I wonder if this pattern is a true picture or if some data issues described above might have played a role? I wonder if a less fine grouping of occupations could tackle this potential problem of comparability of occupational groups over time? Figure 1 is based on a linear slope over time – are there in fact linear trends? In the case of group 9 in men I would suspect a drop when the 4th revision is used. Occupational groups 10 and 11 are left out of some analyses without much rationale. Could this bias the results as some areas might have a larger % of these two groups? Especially group 10 “unclassifiable” has a remarkably high mortality. This group is small

	(less than 1.52 %) so possibly not a big problem to leave this group out, but unemployed is a very large group in women (40-50%). Age group is restricted to 25-64 to exclude students and retired. I guess some students and retired are still included? To be more sure possibly an even narrower age group (30-60) could be used? Minor: Make it clearer that numbers of deaths for each cell are recorded during 1 calendar year. Results answer the research question, but as earlier stressed, the results rely on relative inequalities (except from fig 1 and 2, where mean predicted mortality on logit scale is presented). Authors also have made a set of supplementary analyses accompanied of supplementary text, tables and figures. The amount of information is large and I am not sure if the supplementary analyses are needed in this paper – maybe they could be placed in a separate paper? As authors say the results contras health inequalities across occupational groups described in other industrialized western European and North American countries. It also contrasts a previous study from Japan (Fukada et al, ref no 25) using income, where absolute inequalities have narrowed since 1950s with a flattening out from 1995 to 2005 (or possibly increasing). Saying that this is consistent with findings in this paper seems odd. References are up to date and relevant. Abstract, summary, key messages and what this paper adds reflect accurately what the paper says.

VERSION 1 – AUTHOR RESPONSE

Responses to Reviewers' Comments

Dear Professor Goldblatt,

Thank you very much for your thoughtful review and positive evaluation of our article. We revised our manuscript according to your helpful suggestions.

1. **This paper is welcome in bringing together information on occupation and prefecture of residence from death registration at working ages across a 35 year period for the whole of Japan. Trend data presented on the change in occupational distribution and in patterns of mortality over this period are extremely valuable, as is the analysis of the inter-relationship between occupation, prefecture and social factors. However the findings are difficult to interpret and there are some key questions about the methods used and definitions which are not clear from the paper. These issues are explained in more detail below. Greater clarity about these issues is required before publishing what are on the face of it some extraordinary findings.**

Response:

Thank you very much for your positive evaluation of our article. We thoroughly revised the manuscript following your helpful suggestions. We hope that the revision provides the findings more clearly.

2. Methods and definitions: The social information in this study appears to derive from a comparison of major occupational groups as recorded at death and compared with Census denominators. There are two issues here. First occupational classifications, on their own do not equate to social classifications. To arrive at a social classification from an occupational classification requires two further steps. Firstly, identifying the status in employment of the individual - do they manage or supervise others in the occupational group. Secondly, the occupation and status combination needs to be graded according to the predominant type of employment contract for that combination (e.g. salaried, weekly wage, etc.). It does not appear that this has been carried out for the data used in the article. Clarification of this is essential - is this purely an occupation mortality analysis or is it an analysis according to social position?

Response:

Thank you for your thoughtful comment. One of the aims of this study was to examine the social inequality of all-cause mortality in Japan, and we intended to use occupations as an indicator of socioeconomic position. Generally, previous studies have used occupations, income, education, or wealth as indicators of socioeconomic position, and we understand that there is no single best indicator. Unfortunately, neither the status in employment nor the predominant type of employment contract was available in the present data set, and we briefly mentioned this as a limitation in the DISCUSSION section of the original version. In accordance with your suggestion, we changed “social inequality” to “occupational inequality” throughout the main text when appropriate. Furthermore, we modified sentences in the INTRODUCTION and DISCUSSION section as follows:

(Page 6, lines 6-9)

In this study, by using occupations as an indicator of socioeconomic position,[14] we examine the trends in occupational and geographic inequalities of all-cause premature adult mortality from 1970 through 2005.

(Page 19, lines 9-13)

First, although we were able to conduct a fairly detailed analysis of trends by occupational class, neither the status in employment nor the predominant type of employment contract was available, and in particular, we lacked information on whether the individuals were in standard jobs or precarious jobs.

The second issue concerns the method of data collection. Is there any potential for numerator denominator bias between the two sources of information (census and death)? Specifically, what questions are asked on the two occasions and who are the respondents on the two occasions? In most cross-sectional occupational studies, discrepancies in either or both of these respects lead to numerator denominator bias. The extent of this is not clear from the paper. Nor is it clear from the paper whether any studies have been carried out in Japan to quantify any biases (either longitudinal follow up of census or retrospective in-depth surveys based on death records). Specific issues are whether, by the time a person dies they are either no longer in the occupation recorded for them at

Census or whether the person recording the death either promotes the deceased to a higher status job or demotes them because they did not know the details of their job). As a simple example, it is not uncommon for those in lower status jobs to be selected out of the workforce due to ill health and be recorded as not employed or not classified at death, depending on the question asked at death.

Response:

Thank you for your helpful comment. We agree that the potential for numerator denominator bias is an important issue. In the notification of deaths, the respondents are asked to fill in the occupation of decedent at the time of death, and one of the following persons are obliged to submit the notification: (1) relatives who live together with decedents, (2) other housemates, (3) landlord, estate owner, land/house agent, or (4) relatives who do not live together with decedents. In the questionnaire for the Census, the occupation was assessed by asking a following question: "Description of work – Describe in detail the duties you are assigned to perform." The questionnaires are delivered to each household, and someone of each household answers the question. In accordance with your comment, we added sentences as follows:

(Page 6, line 18 – page 7, line 4)

In the notification of deaths, the respondents are asked to fill in the occupation of decedent at the time of death,[17] and one of the following persons is obliged to submit the notification: (1) relatives who live together with decedents, (2) other housemates, (3) landlord, estate owner, land/house agent, or (4) relatives who do not live together with decedents.

(Page 8, lines 6-9)

In the questionnaire for the Census, the occupation was assessed by asking a following question: "Description of work – Describe in detail the duties you are assigned to perform".[19] The questionnaires are delivered to each household, and someone in each household answers the question.

We are not aware of any studies from Japan that have quantified the numerator denominator bias. We also agree that the possibility of measurement error of occupation at the time of death cannot be ruled out. In accordance with your comment, we added sentences to mention this as a limitation of the present study as follows:

(Page 20, lines 6-12)

Third, considering the possible discrepancies of the respondents on the two occasions (i.e., the notification of deaths and the census), we should note the potential for numerator denominator bias between the two sources of information. In particular, the possibility of measurement error in occupation at the time of death cannot be ruled out – the person recording the notification of deaths may either promotes the deceased to a higher status job or demotes them because the respondents did not know the details of the deceased's job.

3. **Mortality levels: The odds ratios shown in Table 1 are startling. A four-fold difference in mortality for men classified to an occupation and a 16-fold difference for women. Furthermore, most of the substantial differences recorded are in the opposite direction to those seen in longitudinal data in the West. If true, this would imply a catastrophic loss of life in higher status social groups in Japan. However, although the paper looks at several possible explanations (stress, lifestyles, behaviours) it does not identify any biologically plausible explanation for this phenomenon. In terms of previous knowledge, is there a major threat to job security among the best-off in Japanese society? Do they suffer from effort-reward imbalance or a lack of control in their lives or jobs? No evidence or plausible hypothesis is proposed in the paper.**

Response:

We agree that the present findings may well imply a catastrophic loss of life in higher status social groups in Japan. We thoroughly reviewed previous studies from Japan using nationally representative samples. As we explain in the main text, however, the pattern of health inequality in the present analysis is not consistent with previous findings of occupational class differences in health behaviors or psychosocial stress. Although we agree that biologically plausible explanations could strengthen our discussion, we refrained from making specific biologic explanations given our overall outcome (i.e., all-cause mortality). We hope that our discussion reflects properly the present findings.

4. **Geographic differences: The paper identifies some significant differences in mortality across Japan, with some interesting time trends. However, it does not present clear social and other correlations to help explain these patterns and trends. Part of the difficulty may be that, as the paper suggests, the prefectures are so large that they subsume as much within area social and mortality variation as exists between prefectures. If so, the observed patterns may simply be an illustration of the well-known ecological fallacy. A second problem may be that the paper, as noted above, has not identified a biologically plausible explanation for overall social inequalities in mortality. Without this modelling of the interaction between social factors, geography and mortality may be over-ambitious.**

Response:

We fully agree that the prefectures could be so large to explore geographic inequalities. As we explain in the main text, however, the prefecture may be a useful and valid unit of analysis since it is the unit that has direct administrative authority in the economic, education, and health sectors. Furthermore, the prefecture has specific jurisdiction over health centers, which is the locus of preventive health care activity in Japan. We also note that the boundaries between prefectures have not changed since 1867, enabling long-term analysis. In addition, as we explain in the supplementary text, a previous review article suggested that the studies in income inequality are more supportive in larger areas. As you indicated, the potential ecological fallacy could be generally a critical issue in ecological studies. As we explain in the main text, however, the unit of analysis of the present study was “cell” (tabulated by sex, age, occupation, year, and prefecture), and we used proportion of mortality in each cell as an outcome variable. By so doing, the present study examined the population-level association between occupation and mortality and how it varies across prefectures. In other words, we have no ecological X and Y and only individual X and Y. Therefore, we think that the observed patterns are not an illustration of the ecological fallacy.

Dear Dr. Strand,

Thank you very much for your thoughtful review and positive evaluation of our article. We revised our manuscript according to your helpful suggestions.

1. **This is an interesting and well written piece of work extending the existing literature on social inequality mortality trends to also cover Japan. Previous studies on this topic have mainly focused on Western populations. This work is of importance to researchers and policymakers and might be well suited for a general medical journal like BMJ. Research questions are clearly defined. Furthermore, the design of the study is appropriate and by using multilevel methods they ensure to properly adjust for micro- macrolevel bias, as the author Subramanian earlier have described in his paper with Duncan and Jones (Environment and Planning A 2001, volume 33, pages 399-417). Nevertheless, I still miss some basic numbers; for example age adjusted mortality rates by occupational class by year and gender. Such numbers are modeled in Figure 1 and 2, but I suspect the linear trends might be too simplistic, and would like to get an idea of the background numbers before they are run through complicated models. I believe some readers of BMJ will find such multilevel models rather complicated. Data is census based and covers the whole of Japan so exclusion criteria are not highly relevant here. Participants are adequately described.**

Response:

Thank you very much for your positive evaluation of our article. We also appreciate your comment on our analytic methods to properly adjust for micro- and macro-level bias. We thoroughly revised the manuscript following your suggestions, and we created a new table showing the age-adjusted mortality rates by occupational class by year and gender (Supplementary Table 5). We hope that the revision provides the reader with better understanding of the findings.

2. **The multilevel approach is a nice one as commented on above, but the choice of logit link function limits the results to the relative scale presented to the reader as odds ratios. The inequality literature has stressed the importance to also investigate absolute inequalities (see for example Oakes & Kaufman, Methods in social epidemiology, 2006). This is of special importance when looking at mortality trends as rates tend to decline over time and one can have the situation that all socioeconomic groups decrease their rate at similar pace, thus absolute differences are constant, but the relative rate will increase. Table 1 shows increasing ORs, but I suspect this fallacy just described could be the reason for this? Would it be possible to run the model using identity link and get RD?**

Response:

We fully agree with the importance of investigating absolute as well as relative inequalities. As indicated in your comment No. 7, our intention of showing Figures 1 and 2 was to visualize the absolute inequality across occupations. In accordance with your comment, we calculated the age-adjusted mortality rates by occupational class by year and gender (Supplementary Table 5), which we believe will help readers to understand the present findings from absolute as well as relative perspectives. Although we appreciate your suggestion to run the model using identity link function, we think that logit link function is more appropriate in the present analysis, considering that the outcome of interest is the proportion of mortality in each cell. In accordance with your comment, we added sentences as follows:

(Page 9, lines 1-6)

For the descriptive purpose, we first calculated age-adjusted mortality rates by occupational class by year and sex (Supplementary Table 5). We used the direct method, using the model population of 1985 as a reference.[20] The model population of 1985 is based on the Japanese population under census of 1985 and it is created on the basis of 1,000 persons as 1 unit, after adjusting radical increase or decrease such as baby boom.[21]

3. **I have a concern regarding the revision of the classification of occupations and comparability of the 11 groups over time. For example, in group 9 "Production process and related workers" mining workers were included until 1986, but not in the last revision. I suspect mining workers have high mortality rate which could result in group 9 getting higher mortality in the earlier periods. Could this and other changes in the classification affect the results? I especially think of the pattern seen in Figure 1, where some groups, among them group 9, have a rather steep mortality decline. The pattern in men is somewhat strange as lines cross, putting high mortality occupational groups in 1970 among the lowest in 2005 (Sales workers). In women the picture is more harmonized, with decline in mortality in all groups (fig 2). I wonder if this pattern is a true picture or if some data issues described above might have played a role? I wonder if a less fine grouping of occupations could tackle this potential problem of comparability of occupational groups over time? Figure 1 is based on a linear slope over time – are there in fact linear trends? In the case of group 9 in men I would suspect a drop when the 4th revision is used.**

Response:

We agree that mining workers are expected to have a high mortality rate. Indeed, in the fourth revision of the Japan Standard Occupational Classification (Supplementary Table 1), "Production process and related workers" includes mining workers. Please note that, as we cite in the main text, this point is clearly explained in the following website.

(Reference No. 18)

Ministry of Internal Affairs and Communications. Japan Standard Occupational Classification. http://www.stat.go.jp/english/index/seido/shokgyou/index-co.htm.

To clarify this, we added a following sentence in accordance with your comment:

(Page 7, lines 13-14)

Note that the group "production process and related workers" includes mining workers.

We also agree that the time trend of social inequalities among men could be surprising since lines cross (Figure 1), and we appreciate your suggestion of using a less fine grouping of occupations. As explained in the main text, however, our study used occupation (major group) of the Japan Standard Occupational Classification, which yields reasonably consistent occupational grouping throughout the study period. (As noted above, mining workers are consistently categorized as production process

and related workers.) We are thus concerned that using a less fine grouping of occupations does not necessarily present a true picture of the trend of social inequalities. In line with this, Greenland and Rothman suggested that "some categories may be collapsed together when data are sparse, provided these combinations do not merge groups that are very disparate with respect to the phenomena under study" (Greenland S, Rothman KJ. Fundamentals of epidemiologic data analysis. In: Rothman KJ, Greenland S, Lash TL, editors. *Modern Epidemiology*. 3rd ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2008:213-37). After considering your comment very carefully, we decided to use the current occupational grouping. We hope that you agree with this revision.

4. **Occupational groups 10 and 11 are left out of some analyses without much rationale. Could this bias the results as some areas might have a larger % of these two groups? Especially group 10 "unclassifiable" has a remarkably high mortality. This group is small (less than 1.52%) so possibly not a big problem to leave this group out, but unemployed is a very large group in women (40-50%).**

Response:

Thank you for clarifying this. In the whole analysis of the present study, we included occupational groups No. 10 (i.e., workers not classifiable by occupations) and No. 11 (i.e., non-employed). To enhance readability of Figures 1 and 2, however, we excluded them from these Figures. We apologize for the unclear explanation. In accordance with your comment, we added a sentence as follows:

(Page 12, lines 7-8)

We excluded workers not classifiable by occupation and non-employed from these Figures to enhance readability although they were included in the analysis.

5. **Age group is restricted to 25-64 to exclude students and retired. I guess some students and retired are still included? To be more sure possibly an even narrower age group (30-60) could be used?**

Response:

We agree that some students and retired are still included in the study subjects. However, almost all the university students in Japan graduate from universities in their early 20s, and it is getting common to rehire staff of retirement age. Therefore, we believe that the current age restriction reasonably succeeded in excluding students and the retired. If they should be included in the study subjects, they are categorized as "non-employed", and we deliberately avoided giving an interpretation to the result among them in the present article. Also, please note that a previous study from the US also chose age 65 as a cut-off point for premature mortality (Krieger N, Rehkopf DH, Chen JT, Waterman PD, Marcelli E, Kennedy M. The fall and rise of US inequities in premature mortality: 1960-2002. *PLoS Med* 2008;5:e46. doi:10.1371/journal.pmed.0050046). We hope that the current age restriction is appropriate to examine the premature adult mortality.

6. **Minor: Make it clearer that numbers of deaths for each cell are recorded during 1 calendar year.**

Response:

In accordance with your suggestion, we added a sentence as follows:

(Page 8, line 18 – page 9, line 1)

Note that the numbers of deaths for each cell are recorded during one fiscal year.

7. Results answer the research question, but as earlier stressed, the results rely on relative inequalities (except from fig 1 and 2, where mean predicted mortality on logit scale is presented). Authors also have made a set of supplementary analyses accompanied of supplementary text, tables and figures. The amount of information is large and I am not sure if the supplementary analyses are needed in this paper – maybe they could be placed in a separate paper?

Response:

Thank you for your positive evaluation of our article. In accordance with your comment, the revision provides age-adjusted mortality rates by occupations (Supplementary Table 5). Also, please note that our analysis of geographic inequalities assessed the trend of absolute health inequalities quantitatively (Table 2). We believe that, with these modifications, readers can understand the present findings of health inequalities from absolute as well as relative perspectives. We understand that the amount of information provided in the supplementary materials may be large. In this study, we intended to assess the time trend of health inequality in Japan comprehensively (i.e., both socially and geographically). Although this information could be placed in a separate paper, we believe that the comprehensive report may well facilitate understanding of the present findings.

8. As authors say the results contrast health inequalities across occupational groups described in other industrialized western European and North American countries. It also contrasts a previous study from Japan (Fukada et al, ref no 25) using income, where absolute inequalities have narrowed since 1950s with a flattening out from 1995 to 2005 (or possibly increasing). Saying that this is consistent with findings in this paper seems odd.

Response:

We think that you are probably mentioning an ecological study by Fukuda et al. (Fukuda Y, Nakao H, Yahata Y, Imai H. Are health inequalities increasing in Japan? The trends of 1955 to 2000. *Biosci Trends* 2007;1:38-42). Please note that this paper was cited as a reference No. 31 in the original version, and currently it is cited as a reference No. 35. As you indicated, they assessed the time trend of geographic health inequalities in Japan, by examining the association of life expectancy and age-adjusted mortality with per capita income of prefectures and municipalities. We cited their work here since their results are somewhat consistent with ours in the sense that they suggested geographic health inequalities appeared to increase from 1995 to 2000. In accordance with your suggestion, we modified the sentences as follows:

(Page 18, lines 7-13)

By applying the novel multilevel methods, the present study shows that geographic inequalities in premature mortality have also widened since 1995, In an ecological study, Fukuda et al.[35] assessed the time trend of geographic health inequality in Japan, by examining the association of life expectancy and age-adjusted mortality with per capita income of prefectures and municipalities. While excluding Okinawa prefecture from the analyses, they found a possible increase in geographic health inequalities from 1995 to 2000, following a decrease from 1955 to 1995.[35]

9. References are up to date and relevant. Abstract, summary, key messages and what this paper adds reflect accurately what the paper says.

Response:

Thank you very much for your positive evaluation of our article.

We thank 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.

VERSION 2 – REVIEW FOR BMJ OPEN

REVIEWER	Peter Goldblatt Deputy Director Institute of Health Equity Department of Epidemiology and Public Health University College London United Kingdom No competing interests
REVIEW RETURNED	16/12/2011

RESULTS & CONCLUSIONS	The paper is much improved on the previous version. However the authors have pointed out in response to concerns that no previous validation has taken place of the consistency of occupation recording between Census and death. This study therefore provides evidence of some real concerns over this consistency - extremely large mortality ratios for some groups, outside the range seen in linked data studies elsewhere. Rapid changes in the occupational structure of Japan give plausibility to these ratios resulting from differential recording at Census and death, rather than solely being due to hazards associated with work or social conditions. These are important findings and the authors should be forthright in explaining the issues.

REVIEWER	Bjørn Heine Strand, researcher, Norwegian Institute of Public Health, Norway. I have no competing interests.
REVIEW RETURNED	28/11/2011

GENERAL COMMENTS	Thank you for this revised version of the manuscript. The authors have responded well to my comments, and I have not many further

	comments on the paper. I believe it can be published in BMJ Open. I appreciate that they included supplementary table 5. I made a plot of the numbers in tab 5 and it gives basically the same impression as Fig 1. This table gives me more feel about the data and readers without deep knowledge of the more complex multilevel approach can follow. Nevertheless, I am still puzzled by the results. As I commented earlier, some of the lower male occupational groups have a very steep mortality decline, while higher occupational groups have a flat pattern over time. For example sales workers go down from 547 deaths per 100,000 py in 1970 to 113 in 2005. Clerical and production process workers also have an impressive mortality decline, while administrative workers actually increased mortality rate from 233 to 241. These trends are interesting and are reported in the results and in the discussion, but I would like even more discussion about this and some suggestion for explanation for why the fall in mortality has mainly happened among the lower occupational classes. Why has there been such improvement in these groups but not in the higher occupational groups? It seems like health related risk behavior follows the traditional gradient seen in western countries so this cannot be the explanation. The authors mention that the results emerge at the same time as the collapse of the "economic bubble" in the early 1990s. This is interesting, but no further explanation is given. Why does the economic bubble make mortality for sales, clerical and production process workers go down?

REVIEWER	Myoung-Hee Kim (deputy director, People's Health Institute, South Korea) I have nothing to be declared for competing interests.
REVIEW RETURNED	13/11/2011

GENERAL COMMENTS	**Reviewer's comment** This paper is interesting to show that there have been social/geographic mortality inequalities in Japan with the highest level of health in the world, using three-level multilevel analysis. However, there are some points to be clarified or explained further. 1. Occupation has dual implication regarding health inequalities. First, it is an important indicator of socioeconomic position to reflect a relative position based on status/prestige or skill (qualification) in a social hierarchy, which means that it influences the opportunities to access health resources or to avoid health hazards. Second, it has a specific health effect, such as chemical hazards among shoemakers or ergonomic hazards among cashers. Further, in terms of socioeconomic position, occupation should be distinguished from the employment status such as employers, employees, self-employers, and unemployed. However, it's not clear how the occupation category was conceptualized in this study. The authors used the term 'workers – do they mean 'economically active population' as a whole or 'people employed by others'? In general, the latter is used in contrast to employers and selfemployers. In addition, it's hard to identify an assumed hierarchy across occupations; for example, do service or security workers have better

	position compared to production workers? What kinds of jobs are classified as security workers? Further, how can the usual categorization of manual/non-manual or white/blue/pink-collar jobs be applied to these occupations? Socioeconomic inequalities in health matter because they reflect the unequal or unfair structure of the society. Accordingly, health inequalities should be dealt in this context, rather than to show quantitative differences between various social groups. The authors had better present the underlying structure of social/geographic inequality in Japan and potential links between them and health inequalities, accordingly. 2. Along this line, many industrialized countries experienced widening mortality gaps with absolute decline of mortality, because mortality reduction has been more salient among higher socioeconomic groups. However, it seems that it's not the case in Japan. Why? Is there any possibility that the measurement issue (i.e., occupation classification) is related with this phenomenon? The authors should give further explanation for this. The discussion (pp.17) does not give any information but just say that it's not consistent with previous studies. 3. The authors should give clear explanation for tables. Is the Table 1 based on multilevel model or uni-level? If the latter was correct, standard errors were likely to be underestimated. Rather, if the former is correct, random coefficients should be presented together in the table. (Also, the results based on multi-level modeling to include socioeconomic variables at prefecture level had better be presented in the manuscript rather than in the supplementary) 4. In addition, the results should be interpreted more cautiously. For example, the authors stated 'the degree of occupational inequality increased in both sexes' (pp.11), based on the widening of odds ratio between the lowest and the highest groups. I'm not sure it can be said so without considering the overall dispersion across several groups – what if the differences between the remaining groups remain the same or decrease while the gap widens only between the both extremes. 5. Similarly, the authors stated the 'common ecologic effect of place' from the multilevel modeling (pp.18). However, age and occupation were the only variables to be considered at an individual-level. Therefore, we cannot avoid the residual confounding at prefecture level, for example, education, which means that the seemingly contextual effect might be an omitted compositional effect. 6. In addition, the authors suggested that the widening social/geographic inequality in premature adult death after 1990s might be associated with economic recession - "lost two decades following the collapse of the asset bubble". Then, is there any supportive evidence that social and geographic inequalities such as income inequality or regional GDP gap have been aggravated? Economic downturn itself is not a factor to widen inequality, while even economic boom could result in more unequal distribution of resource. As a whole, the authors should give more specific explanation based on the conceptual framework and supportive evidence.

VERSION 2 – AUTHOR RESPONSE

Dear Dr. Kim,

Thank you very much for your thoughtful review and positive evaluation of our article. We revised our manuscript according to your helpful suggestions.

This paper is interesting to show that there have been social/geographic mortality inequalities in Japan with the highest level of health in the world, using three-level multilevel analysis. However, there are some points to be clarified or explained further.

Response:
Thank you very much for your positive evaluation of our article. We thoroughly revised the manuscript following your helpful suggestions. We hope that the revision provides the findings more clearly.

1. Occupation has dual implication regarding health inequalities. First, it is an important indicator of socioeconomic position to reflect a relative position based on status/prestige or skill (qualification) in a social hierarchy, which means that it influences the opportunities to access health resources or to avoid health hazards. Second, it has a specific health effect, such as chemical hazards among shoemakers or ergonomic hazards among cashers. Further, in terms of socioeconomic position, occupation should be distinguished from the employment status such as employers, employees, self-employers, and unemployed. However, it's not clear how the occupation category was conceptualized in this study. The authors used the term 'workers – do they mean 'economically active population' as a whole or 'people employed by others'? In general, the latter is used in contrast to employers and self-employers. In addition, it's hard to identify an assumed hierarchy across occupations; for example, do service or security workers have better position compared to production workers? What kinds of jobs are classified as security workers? Further, how can the usual categorization of manual/non-manual or white/blue/pink-collar jobs be applied to these occupations? Socioeconomic inequalities in health matter because they reflect the unequal or unfair structure of the society. Accordingly, health inequalities should be dealt in this context, rather than to show quantitative differences between various social groups. The authors had better present the underlying structure of social/geographic inequality in Japan and potential links between them and health inequalities, accordingly.

Response:
Thank you very much for your thoughtful comment. We agree that occupation has dual implications regarding health inequalities, and we also note that occupational hazards often overlaps with socioeconomic position since most occupational exposures carrying a risk for health tend to occur among groups of lower socioeconomic position. One of the aims of this study was to examine the social inequality of all-cause premature mortality in Japan, and we intended to use occupations as an indicator of socioeconomic position, as has been explained at the end of the Introduction section. Generally, previous studies have used occupations, income, education, or wealth as indicators of socioeconomic position, and we understand that there is no single best indicator. We fully agree that, in terms of socioeconomic position, occupations should be distinguished from the employment status. As we have explained as a first limitation of the present study, however, neither the status in employment nor the predominant type of employment contract was available in the present data set. Throughout the manuscript, we use the term "workers" following the Japan Standard Occupational Classification, and they mean economically active population. In accordance with your comment, we revised the sentences in the Discussion section as follows:

(Page 21, line 12 – page 22, line 7)
First, although we were able to conduct a fairly detailed analysis of trends by using occupations to measure certain aspects of socioeconomic position, neither the status in employment nor the predominant type of employment contract was available, and in particular, we lacked information on

whether the individuals were in standard jobs or precarious jobs. Given the conspicuous increase in the proportion of the labor force engaged in non-standard work,4 as well as mounting evidence that precarious work is associated with worse health,43 future work needs to examine whether the changing character of the workforce in Japan is contributing to widening health inequalities. The use of more detailed indicators of socioeconomic position would provide further insight into the social inequalities of health. Indeed, greater attention to the theoretical as well as empirical aspects of measurement of socioeconomic position will likely enhance the rigor of research on occupational health inequalities, which would increase the possibility for meaningfully comparing results across studies.44

We acknowledge that it is hard to identify an assumed hierarchy across occupations in this study, and in line with this, Harper and Lynch noted that there is inherently more ambiguity in the ranking of occupations, compared with education and income (Harper S, Lynch J. Measuring health inequalities. In: Oakes JM, Kaufman JS, editors. Methods in Social Epidemiology. San Francisco, CA: Jossey-Bass, 2006:134-68). Furthermore, Galobardes et al. noted that the decrease in manual occupations with concomitant increase in low-level service occupations has altered the stratification that occupation generates in terms of socioeconomic position, and so classification such as manual and non-manual worker may lose some of their meaning in economies which include a large number of low-paid, non-manual service jobs (Galobardes B, Shaw M, Lawlor DA, Davey Smith G, Lynch J. Indicators of socioeconomic position. In: Oakes JM, Kaufman JS, editors. Methods in Social Epidemiology. San Francisco, CA: Jossey-Bass, 2006:47-85). Then, we recognize that the typical occupational hierarchy does not necessarily apply to the occupation (major group) of the Japan Standard Occupational Classification. However, we believe that the occupational classification in the present study yields reasonably consistent occupational grouping throughout the study period. We are thus concerned that using a less fine grouping of occupations does not present a true picture of the trend of social inequalities. Greenland and Rothman suggested that “some categories may be collapsed together when data are sparse, provided these combinations do not merge groups that are very disparate with respect to the phenomena under study” (Greenland S, Rothman KJ. Fundamentals of epidemiologic data analysis. In: Rothman KJ, Greenland S, Lash TL, editors. Modern Epidemiology. 3rd ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2008:213-37). In accordance with your thoughtful comment, we added sentences in the Discussion section as follows:

(Page 19, line 10 – page 20, line 4)
It is worth mentioning that typical occupational hierarchy does not necessarily apply to the occupation (major group) of the Japan Standard Occupational Classification. Indeed, there is inherently more ambiguity in the ranking of occupations, compared with education and income.39 In addition, as noted by Galobardes et al.,14 the decrease in manual occupations with concomitant increase in low-level service occupations has altered the stratification that occupation generates in terms of socioeconomic position, and so classification such as manual and non-manual worker may lose some of their meaning in economies which include a large number of low-paid, non-manual service jobs. Importantly, the occupational classification in the present study yields reasonably consistent occupational grouping throughout the study period, and each group has a reasonably large data. We therefore examined the time trend of social inequalities by using the finest occupational classification available in the Census.

The full description of each occupational group in the fourth revision of the Japan Standard Occupational Classification is available on-line in English. Accordingly, we added a sentence as follows:

(Page 7, lines 13-14)
(The full description of each occupational group is available on-line in English.18)

2. Along this line, many industrialized countries experienced widening mortality gaps with absolute decline of mortality, because mortality reduction has been more salient among higher socioeconomic groups. However, it seems that it's not the case in Japan. Why? Is there any possibility that the measurement issue (i.e., occupation classification) is related with this phenomenon? The authors should give further explanation for this. The discussion (pp.17) does not give any information but just say that it's not consistent with previous studies.

Response:
As explained in the main text, our study used occupation (major group) of the Japan Standard Occupational Classification, which yields reasonably consistent occupational grouping throughout the study period. Therefore, we believe that the measurement error was unlikely in play. We note, however, that there is a possibility that the "compositions" of each occupational group went through a (substantial) change throughout the study period, which might have led to different patterns of occupational hazards, especially among manual workers. In other words, there is a possibility that work environment among them have improved markedly throughout the study period, which requires less labor load.
We also note that occupation-based socioeconomic position may reflect social networks and psychosocial processes. As has been explained in the Discussion section, however, a recent cross-sectional study in Japan demonstrated that occupation was not significantly associated with psychological distress among men or women by using a nationally representative sample in 2007. Thus, the pattern of health inequalities in the present analysis is not consistent with occupational class differences in psychosocial stress. With regard to social networks, recent research from Japan has emphasized the evaluation of social capital as well as social networks in workplaces to explain variations in workers' health. We thus hypothesized a posteriori that, following the collapse of the economic bubble, workers of higher occupational classes have experienced a breakdown of social cohesion within companies, which could cancel out the potential positive benefits among them.
In addition, as we have briefly explained in the second limitation in the Discussion section, there is a possibility of healthy worker effect among some lower occupational groups. This could be induced by the following two processes; (i) healthy people might have selectively entered these occupations, and (ii) unhealthy workers might have selectively exited these occupations.
In accordance with your suggestion, we added sentences to give further explanations as follows:

(Page 18, line 10 – page 19, line 9)
As a possible explanation for the present findings, we note that occupation-based socioeconomic position may reflect social networks,14 which enables its members to access a wide variety of resources. In this respect, recent research from Japan has emphasized the evaluation of social capital as well as social networks in the workplace to explain variations in workers' health.35-37 We thus hypothesized a posteriori that, following the collapse of the economic bubble, workers of higher occupational classes were more likely to experience a breakdown of social cohesion within companies, which could cancel out the potential positive benefits among them. We also note that there is a possibility that the "compositions" of each occupational group went through a (substantial) change throughout the study period, which might have led to different patterns of occupational hazards, especially among lower occupational groups. In other words, there is a possibility that work environment have improved markedly among them throughout the study period, which now requires less labor load. Finally, a possibility of healthy worker effect cannot be ruled out among some lower occupational groups. This could be induced by the following two processes; (i) healthy people might have selectively entered these occupations, and (ii) unhealthy workers might have selectively exited these occupations. Further studies are warranted to examine these possible explanations of the present findings.38

3. The authors should give clear explanation for tables. Is the Table 1 based on multi-level model or

uni-level? If the latter was correct, standard errors were likely to be underestimated. Rather, if the former is correct, random coefficients should be presented together in the table. (Also, the results based on multi-level modeling to include socioeconomic variables at prefecture level had better be presented in the manuscript rather than in the supplementary)

Response:
We apologize for unclear explanations. The results in Table 1 were obtained from multilevel analyses. We appreciate your suggestion to present the results of random parameters, and we fully agree that this information provide further insight into multilevel analyses. Actually, we have already shown the results of random parameters in Table 2, describing adjusted prefecture-level variance for all-cause premature mortality. In other words, Tables 1 and 2 show the results of fixed part and random part, respectively, from the same multilevel models. We decided to show these results separately to enhance readability. In accordance with your suggestion, we revised sentences to give clear explanations for these Tables as follows:

(Page 11, lines 6-8)
Table 1 shows the results of social inequality of all-cause premature mortality in terms of occupation from overall model as well as year-specific models in multilevel analyses.

(Page 13, lines 9-11)
Note that Tables 1 and 2 are based on the same multilevel models, showing the results of fixed and random parts, respectively.

We also appreciate your suggestion to move the results of multilevel models including prefecture-level socioeconomic variables from the Online Supplement to the main text. We note that, in the BMJ Open, it is recommended that articles do not exceed 4,000 words since exceeding this will impact upon the papers' readability. After considering your comment very carefully, we decided to show these results in the Online Supplement. We hope that you agree with this.

4. In addition, the results should be interpreted more cautiously. For example, the authors stated 'the degree of occupational inequality increased in both sexes' (pp.11), based on the widening of odds ratio between the lowest and the highest groups. I'm not sure it can be said so without considering the overall dispersion across several groups – what if the differences between the remaining groups remain the same or decrease while the gap widens only between the both extremes.

Response:
We appreciate your thoughtful comment. We recognize that there are a number of measures of health inequality and that there appears to be a lack of consensus about how it should be measured. Although some studies have used Slope Index of Inequality (SII) and Relative Index of Inequality (RII) to measure health inequalities, these measures are useful only in the situation where the social group under consideration has a natural ordering, as with education and income groups. In addition, when researchers use these measures, they need to assume that the relationship between social group and health status is linear. All things considered, we have decided not to use these measures, and we have visually shown the time trends of social inequalities of all-cause premature mortality in Figures 1 and 2. These visual representations would help the readers considering the overall dispersion across occupations. We agree that widening odds ratios between the lowest and the highest groups do not necessarily reflect the true picture of dramatic changes of health inequalities, and we have introduced them in the main text as a simple, quantitative measure to show a certain aspect of widening health inequalities. In accordance with your comment, we modified a sentence as follows:

(Page 12, lines 8-9)
The widening social inequalities can be more clearly seen in Figures 1 and 2, which show the

temporal pattern of these occupational inequalities across years.

5. Similarly, the authors stated the ‘common ecologic effect of place’ from the multilevel modeling (pp.18). However, age and occupation were the only variables to be considered at an individual-level. Therefore, we cannot avoid the residual confounding at prefecture level, for example, education, which means that the seemingly contextual effect might be an omitted compositional effect.

Response:
We agree with your comment. We revised the sentences as follows:

(Page 20, lines 14-18)
Note that the present study examined geographic inequalities, conditional on individual age and occupation. The present findings thus provide suggestive evidence of “common ecologic effects” of place where people live,41 although we should note that the seemingly ecologic effects might be due to an omitted compositional effect (e.g., income).

On a related issue, it is more likely that, by using a fairly detailed occupational classification, we could adjust for other omitted compositional variables (e.g., education), to the extent that the cross-tabulation of age and occupation correlate with them. We added a sentence as follows:

(Page 20, lines 4-6)
By using a fairly detailed occupational classification, it is likely that we could adjust for other omitted compositional variables (e.g., education), to the extent that the cross-tabulation of age and occupation correlate with them.

6. In addition, the authors suggested that the widening social/geographic inequality in premature adult death after 1990s might be associated with economic recession - “lost two decades following the collapse of the asset bubble”. Then, is there any supportive evidence that social and geographic inequalities such as income inequality or regional GDP gap have been aggravated? Economic downturn itself is not a factor to widen inequality, while even economic boom could result in more unequal distribution of resource. As a whole, the authors should give more specific explanation based on the conceptual framework and supportive evidence.

Response:
Thank you very much for your helpful suggestion. Following the collapse of the asset bubble in the early 1990s, Japan’s economy has been characterized by persistently low growth accompanied by a marked increase in the number of precarious workers (i.e., non-standard jobs such as part-time and contingent workers), from 1 in 5 employees in the 1990s to 1 in 3 employees by 2005. In addition, Japan now ranks closer to countries such as the United States and the UK in terms of indicators of relative poverty, such as poverty rate and poverty gap. Please note that these points have been addressed in the Introduction and the Discussion sections, as one of the conceptual motivations to conduct this study. Meanwhile, we also recognize that the main purpose here was descriptive since there have been no studies that have attempted to examine this in a comprehensive manner. In accordance with your comments, we thoroughly revised the manuscript to give further discussion on these issues. Furthermore, we also created Supplementary Table 9 to show the time trend of prefecture-level socioeconomic variables used in the present study, which would help readers interpreting the present findings more comprehensively.

Dear Dr. Strand,

Thank you very much for your thoughtful review and positive evaluation of our article. We revised our

manuscript according to your helpful suggestions.

1. Thank you for this revised version of the manuscript. The authors have responded well to my comments, and I have not many further comments on the paper. I believe it can be published in BMJ Open.

Response:
Thank you very much for your positive evaluation of our article.

2. I appreciate that they included supplementary table 5. I made a plot of the numbers in tab 5 and it gives basically the same impression as Fig 1. This table gives me more feel about the data and readers without deep knowledge of the more complex multilevel approach can follow.

Response:
We appreciate your suggestion for creating this Table.

3. Nevertheless, I am still puzzled by the results. As I commented earlier, some of the lower male occupational groups have a very steep mortality decline, while higher occupational groups have a flat pattern over time. For example sales workers go down from 547 deaths per 100,000 py in 1970 to 113 in 2005. Clerical and production process workers also have an impressive mortality decline, while administrative workers actually increased mortality rate from 233 to 241. These trends are interesting and are reported in the results and in the discussion, but I would like even more discussion about this and some suggestion for explanation for why the fall in mortality has mainly happened among the lower occupational classes. Why has there been such improvement in these groups but not in the higher occupational groups? It seems like health related risk behavior follows the traditional gradient seen in western countries so this cannot be the explanation. The authors mention that the results emerge at the same time as the collapse of the "economic bubble" in the early 1990s. This is interesting, but no further explanation is given. Why does the economic bubble make mortality for sales, clerical and production process workers go down?

Response:
Thank you for your thoughtful comment. In accordance with your suggestion, we added sentences to give further discussion on this issue as follows:

(Page 18, line 10 – page 19, line 9)
As a possible explanation for the present findings, we note that occupation-based socioeconomic position may reflect social networks,14 which enables its members to access a wide variety of resources. In this respect, recent research from Japan has emphasized the evaluation of social capital as well as social networks in the workplace to explain variations in workers' health.35-37 We thus hypothesized a posteriori that, following the collapse of the economic bubble, workers of higher occupational classes were more likely to experience a breakdown of social cohesion within companies, which could cancel out the potential positive benefits among them. We also note that there is a possibility that the "compositions" of each occupational group went through a (substantial) change throughout the study period, which might have led to different patterns of occupational hazards, especially among lower occupational groups. In other words, there is a possibility that work environment have improved markedly among them throughout the study period, which now requires less labor load. Finally, a possibility of healthy worker effect cannot be ruled out among some lower occupational groups. This could be induced by the following two processes; (i) healthy people might have selectively entered these occupations, and (ii) unhealthy workers might have selectively exited these occupations. Further studies are warranted to examine these possible explanations of the present findings.38

Dear Dr. Goldblatt,

Thank you very much for your thoughtful review and positive evaluation of our article. We revised our manuscript according to your helpful suggestions.

1. The paper is much improved on the previous version. However the authors have pointed out in response to concerns that no previous validation has taken place of the consistency of occupation recording between Census and death. This study therefore provides evidence of some real concerns over this consistency – extremely large mortality ratios for some groups, outside the range seen in linked data studies elsewhere. Rapid changes in the occupational structure of Japan give plausibility to these ratios resulting from differential recording at Census and death, rather than solely being due to hazards associated with work or social conditions.

Response:
In accordance with your comment, we further revised the sentences to explain the third limitation of the present study as follows:

(Page 23, lines 3-5)
Indeed, rapid changes in the occupational structure of Japan could give plausibility to the extremely large odds ratios resulting from the potential for numerator denominator bias.

2. These are important findings and the authors should be forthright in explaining the issues.

Response:
Thank you very much for your positive evaluation of our article. We appreciate your encouragement.

We thank 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.

VERSION 2 – REVIEW FOR BMJ OPEN

REVIEWER	There are no competing interests Peter Goldblatt Deputy Director UCL Institute of Health Equity Department of Epidemiology & Public Health 1-19 Torrington Place London WC1E 7HB
REVIEW RETURNED	30/01/2012

THE STUDY	
RESULTS & CONCLUSIONS	The paper now includes adequate information in the dis cussion section on the limittaions of the cross0sectional methods used to estimate mortlaity levels of accupational groups. However, these reservations are not reflected in the overall conclusions of the paper and the abstract. In particular these imply that the very high levels for some occupations might be biologically plausible. This is not the case. There is a further plausibility scheck that is not met and should be

	checked or referred to. This is that very small geographic differences are reported. Yet some would be present if there were geographic differences in the distribution of occupation . This can easily be checked by applying occupational mortality rates observed in this study to the geaographic distribution of occupations - to see if these accord with reported levels of mortality in each geographic area.

VERSION 2 – AUTHOR RESPONSE

Dear Dr. Goldblatt,

Thank you very much for your thoughtful review and positive evaluation of our article. We revised our manuscript according to your helpful suggestions.

1. The paper now includes adequate information in the discussion section on the limitations of the cross-sectional methods used to estimate mortality levels of occupational groups.

Response:
We are pleased to hear that our revisions to the limitations on repeated cross-sectional design were satisfactory.

2. However, these reservations are not reflected in the overall conclusions of the paper and the abstract. In particular these imply that the very high levels for some occupations might be biologically plausible. This is not the case.

Response:
We apologize that our conclusions did not fully reflect the findings. In accordance with your comment, we revised a sentence in the Conclusions of the main text, carefully avoiding implying that extremely large mortality ratios are biologically plausible. (In the instructions for authors of the Journal, it is recommended that articles do not exceed 4,000 words. Following the reviewers' comments, we now extensively discuss the limitations of this study in the "Limitations of the study" section, and currently, there are 3,996 words in the main text.)

(Page 23, line 17 – page 24, line 2)
Despite several limitations associated with the use of secondary data, the present findings indicate that both social and geographic inequalities in premature adult mortality have increased during Japan's "Lost Two Decades" following the collapse of the asset bubble.

In accordance with your comment, we also modified a sentence in the abstract. Due to the word limit of the abstract, however, we could only slightly revise the sentence. (Currently, there are 299 words in the abstract, and it should not exceed 300 words.) Thus, to further highlight this point, we also revised a sentence in "Strengths and limitations of this study" in the "Article summary" section.

(Page 3, lines 9-10)
The present findings suggest that both social and geographic inequalities in all-cause mortality have increased in Japan during the last three decades.

(Page 4, lines 12-14)
We lacked information on whether the individuals were in standard jobs or precarious jobs, and a possibility of measurement error in occupation at the time of death cannot be ruled out.

3. There is a further plausibility scheck that is not met and should be checked or referred to. This is that very small geographic differences are reported. Yet some would be present if there were

geographic differences in the distribution of occupation. This can easily be checked by applying occupational mortality rates observed in this study to the geographic distribution of occupations - to see if these accord with reported levels of mortality in each geographic area.

Response:
We appreciate your thoughtful comment. We fully agree that the geographic differences in mortality could be a reflection of the occupational distribution by prefectures. Indeed, as explained in the "Geographic and temporal variation in mortality" in the Discussion section, previous studies (e.g., reference No. 40) examined geographic inequalities without taking account of the compositions (e.g., occupational distribution) of each geographic area, which is subject to the limitation above. Thus, in this study, we decided to use multilevel models to examine time trends in premature mortality by occupational class as well as geographic locality simultaneously. In other words, we examined geographic inequality of premature mortality, conditional on individual age and occupation by using multilevel models (see the first sentence of "Geographic inequality of mortality" in the Results section). Accordingly, the results of the present study show age-occupation-adjusted geographic variations for premature mortality across 47 prefectures (e.g., Supplementary Tables 6 and 7). Following the reviewers' comments, we have carefully revised the main text, the abstract, and the "Article summary" section, attempting to explain the present findings more clearly. We hope that our findings provide some insight into these issues.

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