PEER REVIEW HISTORY

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

ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>Lifestyle-related diseases following the evacuation after the Fukushima Daiichi Nuclear Power Plant accident: a retrospective study of Kawauchi village with long-term follow-up.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTHORS</td>
<td>Ebner, Daniel; Ohsawa, Megumi; Igari, Keiko; Harada, Kouji; Koizumi, Akio</td>
</tr>
</tbody>
</table>

VERSION 1 - REVIEW

| REVIEWER | Akira Sakai  
Dept. of Radiation Life Sciences,  
Fukushima Medical University  
School of Medicine.  
Japan |
<table>
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<tbody>
<tr>
<td>REVIEW RETURNED</td>
<td>14-Mar-2016</td>
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<table>
<thead>
<tr>
<th>GENERAL COMMENTS</th>
<th>The study to investigate how the prolonged evacuation affected the prevalence of lifestyle-related disease is important to perform regular health management of evacuees. However, reviewer would like to ask authors as follows:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>As authors pointed out that the prevalence of hypertension decreased (line 229), many readers would like to know the reason. Authors should discuss it in detail (line 254-256).</td>
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<tr>
<td>2.</td>
<td>Although authors mentioned that social and mental stress in concert with decreased physical activity triggered lifestyle-related disease (line 248-250), why did blood pressure decrease? Reviewer is wondering whether these phenomena are contradictory to each other.</td>
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<td>3.</td>
<td>Reviewer would like to know how stresses induced DM (line 231-233).</td>
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<td>4.</td>
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| REVIEWER | Shuhei Nomura  
Imperial College London, United Kingdom |
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<td>30-Mar-2016</td>
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<tr>
<th>GENERAL COMMENTS</th>
<th>Authors investigated chronic health impacts of Japan's 2011 Fukushima Nuclear power plant accident in long-term perspective.</th>
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The data presented in the paper are useful for preparedness and planning in response to a major nuclear or radiological disaster. Overall, the manuscript is well written and most conclusions are correctly drawn from the results. However, it is necessary to address reviewer’s concerns which describe below.

Major points:

Abstract
Line 8-31: Authors should mention about the disaster. I would write "After Japan's 2011 Fukushima Daiichi Nuclear Power Plant Accident, due to the threat of radiological exposure, evacuation was ordered in Kawauchi Village lying 20 km west of the plant until April 2012."

Line 35-36: “A pre-disaster time period (2008-2010) was categorized for comparison...” – This is not clear. Please rephrase.

Line 37-38: “The out come examined .... and adjusted for confounding factors.” – What authors adjusted were not outcomes (i.e. presence/absence of diseases), but outcome measures (i.e. prevalence of diseases).

Line 39-44: I would present odds ratio here, rather than prevalence, and show results both for 2012 and 2013. Why did not authors present obesity and hypertension?

Line 45-47: "...a universal increase in the lifestyle-related diseases has been triggered by the evacuation” – Authors did not compare the health outcomes between evacuees and non-evacuees, so this conclusion cannot be drawn from the results. It should be unclear this increase was due to the general stress from the disaster, social and environmental change after evacuation, or other underlying evacuation effects.

Introduction
Line 99-110: Evaluation of the pre- vs. post-disaster health should be an objective, not an aim. Authors should state what they hope to achieve through this study. Do authors aim to offer practical or policy implications, or add new insights and significant information over the existing knowledge?

Methods
Line 112: Who are eligible and able to receive the national health screening? general population or other particular subpopulations? If there is limited participation, authors should discuss the constraints posed by this to this study. Authors should also state here if this screening is covered by any health insurance scheme.

Line 126-7: "... self-reported lifestyle-related factors” – Please indicate these were obtained from the interview questions to make a linkage to the 'Interview Questionnaire Analysis' in the results section.

Line 138: "Subject with missing..." – This sentence should be moved to the results section, and authors should (1) present how many individuals (numbers and percentage) were excluded and (2) discuss the difference of the characteristics between included and excluded individuals.

Line 171 Why did not authors adjust for biomarkers, such as BMI,
systolic and diastolic blood pressures, etc., which are important confounding factors.

Line 171-72: I would write "An unstructured correlation structure was used to account for correlation among repeated measures on the same subjects."

Results
Line 179-80: "... 777, 797, 779, 674, and 576 people" – Authors should present proportions these numbers accounted for in the population.

Line 180-1: Please be specific about what the "returnees" indicate. When they returned? How and where did other people (i.e. non-returnees) take the national health screening? Did they receive it somewhere other than in Kawauchi Village? How did authors know who were returnees? based on the basic resident register or family registration system? Because evacuees usually do not declare their change of address to the village/town/city office after their evacuation, the address recorded in the resident registers cannot be used to identify returnees.

Table 1: What do A and B indicate? ANOVA is used to examine any mean differences in age, but was age normally or nearly normally distributed?

Table 2: Why did not authors report information of diet changes and medications, which are described in the method section (line 126-9)?

Table 3: What do A, B, and C indicate?

Line 212: Authors should state that the odds ratios are also adjusted for age and gender.

Discussion
Line 273: "It is conceivable that, if the healthiest individuals..." – This sentence may be misleading. If participants more concerned about their health, with good reason (i.e. attend the health screening because they have poorer health), risks in this sample may overestimate the disaster impact. Or participants more concerned about their health, so attend and get treatment, so have better health than non-participants. It is not clear which direction this bias would work. So, authors should state both these directions.

Conclusions
Line 294: "it appears that regardless of patient return, evacuee health has continued to deteriorate" – Authors did not compare the health outcomes between returnees and non-returnees, so this conclusion cannot be drawn from the results.

Minor points:
Authors use "pre-disaster" and "pre-earthquake" for the same meaning. For their use, please be consistent throughout the text. The same applies to "yearly national health screening", "yearly health consultation", "routine yearly physical exams", and "medical examination".

A figure showing the geographical scope of the evacuation
instructions and the locations of Kawauchi Village, Koriyama City, and Komioka Town, relative to the nuclear power plant, will be helpful for readers.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Akira Sakai
Institution and Country: Dept. of Radiation Life Sciences, Fukushima Medical University School of Medicine, Japan
Competing Interests: I have no competing interests.

The study to investigate how the prolonged evacuation affected the prevalence of lifestyle-related disease is important to perform regular health management of evacuees. However, reviewer would like to ask authors as follows:

1. As authors pointed out that the prevalence of hypertension decreased (line 229), many readers would like to know the reason. Authors should discuss it in detail (line 254-256).

Response: Thank you for your suggestion. We evaluated medication status and other causes for the potential blood pressure decrease, but were unable to elucidate a clear reason. As of now, it remains a mystery. We have modified the paper to reflect this better per your suggestion (L297-306 in change-tracked version).

2. Although authors mentioned that social and mental stress in concert with decreased physical activity triggered lifestyle-related disease (line 248-250), why did blood pressure decrease? Reviewer is wondering whether these phenomena are contradictory to each other.

Response: It is unclear why blood pressure decreased. As you suggest, one might expect hypertension to increase from psychosocial factors, but it did not appear to in those receiving their yearly NHI examinations. Hypertension is well understood by local healthcare teams, and so it is possible that health teams focused on hypertension in survivors in a way that health record evaluation, questionnaires, and follow-up interviewing could not capture.

3. Reviewer would like to know how stresses induced DM (line 231-233).

Response: Unfortunately, the exact mechanisms are outside the scope of this study, which is based on epidemiological data alone. There is literature regarding in vivo models of DM development, but large scale studies would be required to delineate the mechanism by which a population as a whole may develop DM.

4. Reviewer would like to know why poor sleep and mental stress, which authors discussed in line 262, were not causes of hypertension.

Response: Poor sleep and mental stress likely had an impact on the blood pressure of the population, but this change was not seen due to the unknown cause that lead to lowering of blood pressure. Without an ability to identify the cause of the blood pressure decrease, we are unable to hypothesize as to why expected increases were not seen.

5. Reviewer is wondering why lifestyle-related disease increased in the conditions the residents were living have improved (line 266).
Response: Lifestyle-disease may not operate instantaneously, but instead may be a delayed response due to previous stress events. As such, improvement of living conditions in the year of our last measurement, owing to a return to Kawauchi, may cause a reduction in worsening rate, but not an overall improvement in health condition. Further, though residents returned to their home village, Kawauchi itself, as lines 280-296 in change-tracked version describe, is different: many families and particularly younger members of the village did not return, causing a stressor that did not appear pre-disaster. As such, we may expect improvement in the population relative to evacuees, but not a return to pre-disaster levels, as Kawauchi Village itself has not been restored to a pre-disaster state.

6. Did authors think that a lot of compensation costs from Tokyo Electric Power Co. changed the lifestyle of residents? That is the reason of lifestyle-related disease?

Response: We have no data regarding compensation, if any, that residents may have received from TEPCO. However, any financial proceeds from the disaster likely only serves to blunt the psychosocial, socioeconomic, and overall health toll the disaster, evacuation, and ongoing recovery had on the residents.

Reviewer: 2
Reviewer Name: Shuhei Nomura
Institution and Country: Imperial College London, United Kingdom
Competing Interests: None declared

Authors investigated chronic health impacts of Japan's 2011 Fukushima Nuclear power plant accident in long-term perspective. The data presented in the paper are useful for preparedness and planning in response to a major nuclear or radiological disaster. Overall, the manuscript is well written and most conclusions are correctly drawn from the results. However, it is necessary to address reviewer’s concerns which describe below.

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Line 35-36: "A pre-disaster time period (2008-2010) was categorized for comparison..." – This is not clear. Please rephrase.

Line 37-38: "The outcome examined .... and adjusted for confounding factors." – What authors adjusted were not outcomes (i.e. presence/absence of diseases), but outcome measures (i.e. prevalence of diseases).

Response: Thank you for your kind recommendations. We have modified the paper accordingly (L28-41 in change-tracked version).

Line 39-44: I would present odds ratio here, rather than prevalence, and show results both for 2012 and 2013. Why did not authors present obesity and hypertension?

Response: We described obesity and hypertension (L47-48 in change-tracked version).

Line 45-47: "...a universal increase in the lifestyle-related diseases has been triggered by the evacuation" – Authors did not compare the health outcomes between evacuees and non-evacuees, so this conclusion cannot be drawn from the results. It should be unclear this increase was due to the
general stress from the disaster, social and environmental change after evacuation, or other underlying evacuation effects.

Response: Thank you for this comment. You are correct – we have epidemiological data and can hypothesize causes based on known events in the population (disaster, evacuation, return to a recovering village, ongoing psychosocial and socioeconomic fallout of the disaster in the region), but cannot say definitively the evacuation in particular caused these problems. There may be a correlation.

Introduction
Line 99-110: Evaluation of the pre- vs. post-disaster health should be an objective, not an aim. Authors should state what they hope to achieve through this study. Do authors aim to offer practical or policy implications, or add new insights and significant information over the existing knowledge?

Response: Thank you for the comment. We have revised as the reviewer commented (L108 and L113-114 in change-tracked version)

Methods
Line 112: Who are eligible and able to receive the national health screening? general population or other particular subpopulations? If there is limited participation, authors should discuss the constraints posed by this to this study. Authors should also state here if this screening is covered by any health insurance scheme.

Response: The screening was covered by the Japanese National Health Insurance (Line 132-133 in change-tracked version). The total population was eligible.

Line 126-7: "... self-reported lifestyle-related factors" – Please indicate these were obtained from the interview questions to make a linkage to the 'Interview Questionnaire Analysis' in the results section.

Response: Thank you for the comment. We have revised the manuscript so that questionnaires have an independent paragraph (L151-154 in change-tracked version) and are linked to the interview analysis.

Line 138: "Subject with missing..." – This sentence should be moved to the results section, and authors should (1) present how many individuals (numbers and percentage) were excluded and (2) discuss the difference of the characteristics between included and excluded individuals.

Response: We moved the section to the results section. We also provided tables to show the difference of the characteristics between included and excluded individuals (Supplemental Tables S1-7). Most exclusion occurred due to a lack of biochemical testing. There are differences in age and sex within the population, but these are consistent before and after the Fukushima disaster. Therefore, the effect of evacuation is not considered to be affected by missing data. We added this explanation in text (L201-212 in change-tracked version).

Line 171 Why did not authors adjust for biomarkers, such as BMI, systolic and diastolic blood pressures, etc., which are important confounding factors.

Response: Our objective is to compare overall prevalence of lifestyle-related disease before and after the disaster, not the changes of individual parameters. Individual parameter evaluation over a longitudinal timeframe is important, and may constitute future studies.

Line 171-72: I would write "An unstructured correlation structure was used to account for correlation
among repeated measures on the same subjects."

Response: We rewrote manuscript as the reviewer suggested (L192-193 in change-tracked version).

Results
Line 179-80: "... 777, 797, 779, 674, and 576 people" – Authors should present proportions these numbers accounted for in the population.

Response: We revised Table 1 to include total populations in each year. 1205 individuals attended any of examinations. We added this explanation in text (L 213-215 in change-tracked version).

Line 180-1: Please be specific about what the "returnees" indicate. When they returned? How and where did other people (i.e. non-returnees) take the national health screening? Did they receive it somewhere other than in Kawauchi Village? How did authors know who were returnees? based on the basic resident register or family registration system? Because evacuees usually do not declare their change of address to the village/town/city office after their evacuation, the address recorded in the resident registers cannot be used to identify returnees.

Response: We added the explanation (L215-217 in change-tracked version).

Table 1: What do A and B indicate? ANOVA is used to examine any mean differences in age, but was age normally or nearly normally distributed?

Response: We added the explanation in Table 1. The age distributed nearly normally.

Table 2: Why did not authors report information of diet changes and medications, which are described in the method section (line 126-9)?

Response: We revised Table 2 as suggested by the reviewer. Medication status for cholesterolemia significantly changed after the disaster, which resulted from increased prevalence of cholesterolemia. Antihypertension medications did not change in spite of the reduction in blood pressure after the disaster. In addition, dietary habit became irregular. We added this explanation in text (L232-234 in change-tracked version).

Table 3: What do A, B, and C indicate?

Response: The same as the above.

Line 212: Authors should state that the odds ratios are also adjusted for age and gender.

Response: We did (L255-256 in change-tracked version).

Discussion
Line 273: "It is conceivable that, if the healthiest individuals..." – This sentence may be misleading. If participants more concerned about their health, with good reason (i.e. attend the health screening because they have poorer health), risks in this sample may overestimate the disaster impact. Or participants more concerned about their health, so attend and get treatment, so have better health than non-participants. It is not clear which direction this bias would work. So, authors should state both these directions.
Response: We agree with this reviewer on this point (L325-328 in change-tracked version).

Conclusions
Line 294: "it appears that regardless of patient return, evacuee health has continued to deteriorate" – Authors did not compare the health outcomes between returnees and non-returnees, so this conclusion cannot be drawn from the results.

Response: We agree with this reviewer on this point (L346-348 in change-tracked version).

Minor points:
Authors use "pre-disaster" and "pre-earthquake" for the same meaning. For their use, please be consistent throughout the text. The same applies to "yearly national health screening", "yearly health consultation", "routine yearly physical exams", and "medical examination".

Response: We have revised the manuscript with this in mind. Thank you.

A figure showing the geographical scope of the evacuation instructions and the locations of Kawauchi Village, Koriyama City, and Komioka Town, relative to the nuclear power plant, will be helpful for readers.

Response: Thank you for this suggestion. However, we cannot find an appropriate map officially displaying this information. Sorry for not responding your comment.

### VERSION 2 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Akira Sakai</th>
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<tbody>
<tr>
<td>Fukushima Medical University School of Medicine, Japan</td>
<td></td>
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<td>REVIEW RETURNED</td>
<td>16-Jun-2016</td>
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| GENERAL COMMENTS                | Authors responded to my comments accurately. |

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<th>REVIEWER</th>
<th>Shuhei Nomura</th>
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<tr>
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<td>19-Jun-2016</td>
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</table>

| GENERAL COMMENTS                | The paper has now been substantially revised with the answers. In particular, the methods and results sections were well modified.
|                                | Therefore, I would recommend it for acceptance in BMJ Open. |
|                                | Minor point: The number of significant figures should be consistent throughout the text. |