

PEER REVIEW HISTORY

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

ARTICLE DETAILS

TITLE (PROVISIONAL)	Effects of socioeconomic factors on cardiovascular related symptoms among residents in Fukushima after the Great East Japan Earthquake: A cross-sectional study using data from the Fukushima Health Management Survey
AUTHORS	Zhang, Wen; Ohira, Tetsuya; Yasumura, Seiji; Maeda, Masaharu; Ohtsuru, Akira; Harigane, Mayumi; Horikoshi, Naoko; Suzuki, Yuriko; Yabe, Hirooki; Nagai, Masato; Nakano, Hironori; Hirosaki, Mayumi; Uemura, Mayu; Takahashi, Hideto; Kiyama, Kenji; Yamashita, Shunichi; Abe, Masafumi

VERSION 1 - REVIEW

REVIEWER	Misa Takegami National Cerebral and Cardiovascular Center, Japan
REVIEW RETURNED	22-Sep-2016

GENERAL COMMENTS	<p>In the manuscript entitled, 'Association of socioeconomic factors after a disaster with cardiovascular related symptoms: the Fukushima Health Management Survey', the authors present findings of the impact of the Great East Japan Earthquake on the relationship between socioeconomic factors and the cardiovascular health of residents in the evacuation zone, officially determined to be near a nuclear power station.</p> <p>Although the findings are of interest, the appeal is too limited owing to the presentation.</p> <p>The authors defined headache, dizziness, palpitations, and shortness of breath as cardiovascular symptoms, and discussed that the findings of this study were supported by previous reports on the increase of cardiovascular diseases (CVD) after earthquakes.</p> <p>Evidence that is more direct is needed to show that these symptoms affect the incidence of CVD. Without this strong argument, the discussion would not be logical based on the results. Recently, the presence of headache in hypertension was reported to be possibly paradoxically associated with a low risk of CVD (Am J Hypertension, 29: 1109-16, 2016). Thus, it is unreasonable to consider these symptoms as advanced. Rather than viewing these symptoms from the perspective of the risk of CVD, it would be easier to understand these symptoms if viewed as stress and/or autonomic nervous symptoms. The author used post-traumatic stress disorder syndromes in the title of Table 1 (page 24, line 542).</p> <p>Not only the earthquake but also the nuclear accident had a large psychological impact on the subjects in this study. Therefore, this study cannot be unconditionally compared with other studies, which</p>
-------------------------	---

	<p>deal only with earthquakes.</p> <p>Socioeconomic status (SES) in this study was measured based on decreased income, unemployment, and loss of housing as a result of the disaster. SES in this study might vary from its original definition because in this study, unlike in the original definition, income and educational status were not included. Hence, the current text should be amended or a supplemental explanation should be added to avoid any misinterpretation of the content. In particular, additional information would be helpful regarding the second point in the 'Strengths and Limitations' section of this study (page 6, line 101).</p> <p>Moreover, Table 1 provides too much information, which is redundant, and it would be more informative to shorten the text in the table. Please note that the authors should also correct the formatting of Table 1, as it has shifted.</p> <p>I hope that my comments prove useful for the improvement of the article.</p>
--	--

REVIEWER	Sónia Ribeiro North of Lisbon Hospital Center, Lisbon, Portugal
REVIEW RETURNED	01-Oct-2016

GENERAL COMMENTS	<p>this paper is relevant and generally well presented</p> <p>should mention and develop, i think, other important limitations, such as</p> <ul style="list-style-type: none"> - subjectivity of self-response survey, - non presential response and - non-objective assessment of cardiovascular risk factors such as blood pressure.
-------------------------	---

REVIEWER	Anand Irimpen Tulane University Heart & Vascular Institute
REVIEW RETURNED	13-Oct-2016

GENERAL COMMENTS	Appears well designed and very interesting topic.
-------------------------	---

REVIEWER	Hiroaki Shimokawa Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan
REVIEW RETURNED	10-Nov-2016

GENERAL COMMENTS	<p>In the manuscript bmjopen-2016-014077, Zhang et al. reported an inverse relationship between socioeconomic status and exacerbated cardiovascular symptoms after the Great East Japan Earthquake (GEJE). Although the findings were clinically important, there are several comments and concerns.</p> <p>Major comments:</p>
-------------------------	---

	<p>1. The authors defined headache, dizziness, palpitations, and short of breath as cardiovascular symptoms. However, all of them were not necessarily cardiovascular. Although the authors mentioned a possibility that these symptoms could be due to mental distress after GEJE, further discussions are warranted whether these symptoms were just primary psychological symptoms rather than secondary cardiovascular symptoms. In addition, it should be examined whether these symptoms were confounding one another.</p> <p>2. Although the authors claimed an inverse relationship between “low” socioeconomic status and exacerbated cardiovascular symptoms after GEJE, it was unclear how “low” status of socioeconomic circumstances was determined.</p> <p>3. Since sex differences in exacerbation of mental disorder are reported, sub-group analysis by sex may provide important insights.</p> <p>4. Many papers have been published regarding the prognostic and other influences of GEJE (Circ J. 2015;79:664-7; JAMA. 2012;308:667-9; Circ J. 2012;76:1283-85; Eur Heart J 2012; 33: 2796-803; Circ J 2013; 77: 490-3; Circ J 2012; 76:1283-5; N Engl J Med 2013; 369: 2165-7; Am J Cardiol 2013; 112: 94-9; Am J Cardiol 2012; 110: 1856-60; Int J Cardiol. 2015;198:102-5; Circ J. 2015;79(5):1000-8; Am J Cardiol. 2013;112:94-9; Int Heart J. 2014;55:53-7; J Card Fail. 2016 Oct 18. pii: S1071-9164(16)31167-8. doi: 10.1016/j.cardfail.2016.10.003., etc.). In the manuscript, however, few of them were cited and discussed. The authors should cite appropriate papers more and deepen the discussion. In particular, comparison with reports on socioeconomic and psychological impacts of GEJE would be informative.</p> <p>Minor comments:</p> <p>1. In addition to the number of individuals with symptoms, showing their percentages will help the readers to easily understand the impact of GEJE.</p> <p>2. Uploading of Table 1 might have been partly unsuccessful. Please check the overlapping of lines.</p>
--	---

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Misa Takegami

Institution and Country: National Cerebral and Cardiovascular Center, Japan

Please state any competing interests: None declared

Please leave your comments for the authors below

In the manuscript entitled, ‘Association of socioeconomic factors after a disaster with cardiovascular related symptoms: the Fukushima Health Management Survey’, the authors present findings of the impact of the Great East Japan Earthquake on the relationship between socioeconomic factors and the cardiovascular health of residents in the evacuation zone, officially determined to be near a nuclear power station.

Although the findings are of interest, the appeal is too limited owing to the presentation.

The authors defined headache, dizziness, palpitations, and shortness of breath as cardiovascular symptoms, and discussed that the findings of this study were supported by previous reports on the increase of cardiovascular diseases (CVD) after earthquakes.

Evidence that is more direct is needed to show that these symptoms affect the incidence of CVD. Without this strong argument, the discussion would not be logical based on the results. Recently, the presence of headache in hypertension was reported to be possibly paradoxically associated with a low risk of CVD (Am J Hypertension, 29: 1109-16, 2016). Thus, it is unreasonable to consider these symptoms as advanced. Rather than viewing these symptoms from the perspective of the risk of CVD, it would be easier to understand these symptoms if viewed as stress and/or autonomic nervous symptoms.

Yes evidence that is more direct is needed to show that these symptoms affect the incidence of CVD. Unfortunately, the data of incidence of CVD among the evacuees has not been set up yet. Though some studies did not support these symptoms predict CVD. However, there were some other studies showed that the symptoms were associated with cardiovascular problems (Ref 31-34). Therefore, our study of the 4 symptoms may be helpful for improvement of evacuees' health to some extent. We also added this point to limitations (Page 19)

The author used post-traumatic stress disorder syndromes in the title of Table 1 (page 24, line 542). So sorry for the mistake. The title of Table 1 has been revised.

Not only the earthquake but also the nuclear accident had a large psychological impact on the subjects in this study. Therefore, this study cannot be unconditionally compared with other studies, which deal only with earthquakes.

We have added this point as a one of the limitations to the manuscript (Page 19)

Socioeconomic status (SES) in this study was measured based on decreased income, unemployment, and loss of housing as a result of the disaster. SES in this study might vary from its original definition because in this study, unlike in the original definition, income and educational status were not included. Hence, the current text should be amended or a supplemental explanation should be added to avoid any misinterpretation of the content. In particular, additional information would be helpful regarding the second point in the 'Strengths and Limitations' section of this study (page 6, line 101).

Thank you for pointing out that. Some explanation has been added to introduction (Page 7) and educational status has been included in our analysis.

Moreover, Table 1 provides too much information, which is redundant, and it would be more informative to shorten the text in the table. Please note that the authors should also correct the formatting of Table 1, as it has shifted.

Thank you for your suggestion. The title and format of Table 1 has been revised.

I hope that my comments prove useful for the improvement of the article.

Reviewer: 2

Reviewer Name: Sónia Ribeiro

Institution and Country: North of Lisbon Hospital Center, Lisbon, Portugal

Please state any competing interests: None declared

Please leave your comments for the authors below

This paper is relevant and generally well presented

should mention and develop, i think, other important limitations, such as

- subjectivity of self-response survey,

- non presential response and
- non-objective assessment of cardiovascular risk factors such as blood pressure.

Thank you for pointing out these problems. We had added these to the limitations of the manuscript.

Reviewer: 3

Reviewer Name: Anand Irimpen

Institution and Country: Tulane University Heart & Vascular Institute

Please state any competing interests: None declared

Please leave your comments for the authors below

Appears well designed and very interesting topic.

Thank you so much for your encouragement.

Reviewer: 4

Reviewer Name: Hiroaki Shimokawa

Institution and Country: Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine,

Sendai, Japan

Please state any competing interests: None declared

Please leave your comments for the authors below

In the manuscript bmjopen-2016-014077, Zhang et al. reported an inverse relationship between socioeconomic status and exacerbated cardiovascular symptoms after the Great East Japan Earthquake (GEJE). Although the findings were clinically important, there are several comments and concerns.

Major comments:

1. The authors defined headache, dizziness, palpitations, and short of breath as cardiovascular symptoms. However, all of them were not necessarily cardiovascular. Although the authors mentioned a possibility that these symptoms could be due to mental distress after GEJE, further discussions are warranted whether these symptoms were just primary psychological symptoms rather than secondary cardiovascular symptoms. In addition, it should be examined whether these symptoms were confounding one another.

Though some studies did not support these symptoms predict CVD. However, there were some other studies showed that the symptoms were associated with cardiovascular problems (Ref 31-34).

Therefore, our study of the 4 symptoms may be helpful for improvement of evacuees' health to some extent.

We also confirmed that these symptoms were not confounding each other (data not shown).

2. Although the authors claimed an inverse relationship between "low" socioeconomic status and exacerbated cardiovascular symptoms after GEJE, it was unclear how "low" status of socioeconomic circumstances was determined.

Thank you for your comment. We have added some explanation to introduction (page 7)

3. Since sex differences in exacerbation of mental disorder are reported, sub-group analysis by sex may provide important insights.

Sub-group analysis by sex has been conducted and the results has been shown in Table 2.

4. Many papers have been published regarding the prognostic and other influences of GEJE (Circ J. 2015;79:664-7; JAMA. 2012;308:667-9; Circ J. 2012;76:1283-85; Eur Heart J 2012; 33: 2796-803;

Circ J 2013; 77: 490-3; Circ J 2012; 76:1283-5; N Engl J Med 2013; 369: 2165-7; Am J Cardiol 2013; 112: 94-9; Am J Cardiol 2012; 110: 1856-60; Int J Cardiol. 2015;198:102-5; Circ J. 2015;79(5):1000-8; Am J Cardiol. 2013;112:94-9; Int Heart J. 2014;55:53-7; J Card Fail. 2016 Oct 18. pii: S1071-9164(16)31167-8. doi: 10.1016/j.cardfail.2016.10.003., etc.). In the manuscript, however, few of them were cited and discussed. The authors should cite appropriate papers more and deepen the discussion. In particular, comparison with reports on socioeconomic and psychological impacts of GEJE would be informative.

Thank you for providing these papers. We have read them and cited some of them to the manuscript.

Minor comments:

1. In addition to the number of individuals with symptoms, showing their percentages will help the readers to easily understand the impact of GEJE.

Thank you for your advice. Percentages has been shown in Page 11.

2. Uploading of Table 1 might have been partly unsuccessful. Please check the overlapping of lines. Format of Table 1 has been revised.

VERSION 2 – REVIEW

REVIEWER	Sónia Ribeiro North of Lisbon Hospital Center - Portugal
REVIEW RETURNED	10-Jan-2017

GENERAL COMMENTS	This article refers to an important and difficult issue to address i think that after revision, even now reflects the difficulty of applying scientific methods in these circumstances the goal and results are fully understood and in agree with the general purpose of the paper
-------------------------	---

REVIEWER	Hiroaki Shimokawa Tohoku University
REVIEW RETURNED	30-Dec-2016

GENERAL COMMENTS	In the revised manuscript bmjopen-2016-014077/R1, Zhang et al. responded to some comments appropriately, but there remain some issues to be addressed. 1) Although the authors consistently claimed that headache, dizziness, palpitation and short of breath were cardiovascular symptoms, it may be difficult for physicians to primarily consider these symptoms as cardiovascular, without appropriate supporting evidence or differential diagnosis. As the Reviewer #1 pointed out, it is reasonable to understand these symptoms as those related to stress and/or autonomic nervous system disorders, rather than cardiovascular ones, without documentation of other cardiovascular signs, symptoms, or events. Thus, it is not appropriate that these symptoms were treated as cardiovascular throughout the paper with a brief comment on this important issue in the limitation section. 2) The author did not seem to respond appropriately to this comment. They just cited only a few of the suggested papers without any further discussion. Furthermore, it is a pity that they did not cite
-------------------------	---

	a paper reporting the impact of socioeconomic factors on cardiovascular events after the GEJE (Circ J. 2015;79:664-7).
--	--

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Reviewer Name: Sónia Ribeiro

Institution and Country: North of Lisbon Hospital Center - Portugal

Please state any competing interests: None declared

Please leave your comments for the authors below

This article refers to an important and difficult issue to address

i think that after revision, even now reflects the difficulty of applying scientific methods in these circumstances

the goal and results are fully understood and in agree with the general purpose of the paper
Thank you so much.

Reviewer: 4

Reviewer Name: Hiroaki Shimokawa

Institution and Country: Tohoku University

Please state any competing interests: None declared

Please leave your comments for the authors below

In the revised manuscript bmjopen-2016-014077/R1, Zhang et al. responded to some comments appropriately, but there remain some issues to be addressed.

1) Although the authors consistently claimed that headache, dizziness, palpitation and short of breath were cardiovascular symptoms, it may be difficult for physicians to primarily consider these symptoms as cardiovascular, without appropriate supporting evidence or differential diagnosis. As the Reviewer #1 pointed out, it is reasonable to understand these symptoms as those related to stress and/or autonomic nervous system disorders, rather than cardiovascular ones, without documentation of other cardiovascular signs, symptoms, or events. Thus, it is not appropriate that these symptoms were treated as cardiovascular throughout the paper with a brief comment on this important issue in the limitation section.

As you pointed out, the 4 symptoms in the present study would not be logical predict cardiovascular diseases. However, the symptoms was suggestive of risk for CVD. In addition, we also conducted a sub-analyses suggest that all the 4 symptoms were associated with the diagnosis of hypertension in the last year by self-report and exacerbation of dizziness, palpitation and shortness of breath was associated with the diagnosis of heart disease in the last year by self-report among the evacuees (data not shown). Therefore, our study of the 4 symptoms may be helpful for improvement of evacuees' health to some extent.

2) The author did not seem to respond appropriately to this comment. They just cited only a few of the suggested papers without any further discussion. Furthermore, it is a pity that they did not cite a paper reporting the impact of socioeconomic factors on cardiovascular events after the GEJE (Circ J. 2015;79:664-7).

Thanks so much for your recommendation. We have read the paper and cited it.

VERSION 3 – REVIEW

REVIEWER	Hiroaki Shimokawa Department of Cardiovascular medicine Tohoku University Graduate School of Medicine
REVIEW RETURNED	04-Feb-2017

GENERAL COMMENTS	The authors responded to the comments appropriately. There are no further issues to be addressed.
-------------------------	---