

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Impact of disasters, including pandemics, on cardiometabolic outcomes across the life-course: A systematic review
<b>AUTHORS</b>	De Rubeis, Vanessa; Lee, Jinhee; Anwer, Muhammad Saqib; Yoshida-Montezuma, Yulika; Andreacchi, Alessandra; Stone, Erica; Iftikhar, Saman; Morgenstern, Jason; Rebinsky, Reid; Neil-Sztramko, Sarah; Alvarez, Elizabeth; Apatu, Emma; Anderson, Laura

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Koichiro Shiba Harvard T.H. Chan School of Public Health
<b>REVIEW RETURNED</b>	29-Nov-2020

<b>GENERAL COMMENTS</b>	<p>This study is a systematic review of existing literature documenting the link between disaster exposures and subsequent cardiometabolic health. Its focus on the life-course aspect (i.e., timing of exposure) is unique. Based on the review, the authors concluded that any type of disaster exposure is linked to poor cardiometabolic health. Although this is an important topic, the manuscript needs substantial revision as it does not clearly articulate the rationale for the study's aims as it stands. Also, the interpretation of the results is somewhat questionable. Here, I describe some of the specific concerns I have.</p> <p>1. In the Introduction, the authors need to provide more background information with regards to the life-course perspective. They could discuss things like why the impacts of disasters may differ depending on the timing of the exposure, public health implications of reviewing existing evidence from this angle, etc. The current introduction does not give a compelling rationale for the research aim.</p> <p>2. Throughout the manuscript, there seems to be too much emphasis on the ongoing pandemic. I do not think the current study is particularly relevant for the public health strategies for the COVID-19 pandemic. After all, only a few papers they found focused on pandemic and none of them were about the COVID-19 pandemic. Nevertheless, the authors are making strong claims that the findings can inform policies related to COVID-19. For example, the authors wrote the following:</p> <p>"the findings may serve to guide our understanding of expected outcomes and to develop future research to study the effects of COVID-19 on cardiometabolic outcomes. The results from this study can also be used to better understand the trade-off between the implementation of public health measures, such as physical</p>
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	<p>distancing to reduce transmission of a virus, and the implications with access to healthcare, as the review found access to healthcare was limited following a disaster"</p> <p>It was not clear to me which result from this study supports this kind of claim.</p> <p>3. This study focused on the "long-term" effects of disasters on cardiometabolic health. This is an important point to emphasize because there is plenty of evidence documenting the short-term/acute effects of disasters as well. The authors briefly touched on this when they described their search strategy, but stating their focus more clearly would enhance the readability of this paper.</p> <p>4. The reviews revealed that there are mixed findings regarding the associations between disasters and cardiometabolic health. Not all studies reported significant differences in the outcomes by levels of exposure to disasters. Yet, the tone in Discussion is that there was clear evidence that disasters are linked to deteriorated cardiometabolic health. They briefly mentioned potential reasons for the mixed findings (e.g., length of follow-up), but did not sufficiently discuss other explanations (e.g., the difference in disaster type, definitions of "disaster exposures", what comparison was being made).</p> <p>5. More discussion on study limitations is needed.</p>
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<b>REVIEWER</b>	Bazoukis, George Geniko Nosokomeio Athenon o Euangelismos
<b>REVIEW RETURNED</b>	16-Dec-2020

<b>GENERAL COMMENTS</b>	<p>The authors presented a systematic review to determine the impact of disasters, including pandemics, on cardiometabolic outcomes across the life-course. It is a well written study reported the conflicting results of the different studies, However, while a meta-analysis would be helpful, the heterogeneity of the data reported makes the quantitative synthesis not feasible.</p> <p>Comments:</p> <p>In the study selection, data extraction section and critical appraisal sections, you mention that two independent reviewers and abstractors worked but you report several names. It is not clear what was the contribution of the authors or the way that the authors worked on this task.</p> <p>Table 1 can be included as a supplementary file and not in the main text.</p> <p>In the table 3, it must be clear that the effect estimated in the last column are associated with the numbers of the outcomes in the previous column.</p> <p>A limitations section is required following the discussion section according to PRISMA statement.</p>
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<b>REVIEWER</b>	JL Mehta University of Arkansas for medical sciences/VA Medical center
<b>REVIEW RETURNED</b>	03-Feb-2021

<b>GENERAL COMMENTS</b>	<p>An interesting article.</p> <p>In my opinion, the greatest strength of the article is the concept and timeliness of the study. Another strength is the in-depth and transparent description of the research methodology.</p> <p>Some weaknesses of the study are the heterogeneity of the population, which is well addressed by the organization of results by natural vs man-made and adult vs childhood exposures. While the results could not be compared between studies due to the heterogeneity, it would be interesting to see similar studies which have similar exposures and populations compared. I would further recommend fragmentation of the paragraphs in the results section so dissimilar observations can be separated to aid the flow of reading. I would also recommend a more detailed postulation of possible mechanisms in the discussion. Furthermore, is there a difference between outcomes of exposures related to the neurobiological axis (e.g. greater stress) and exposures leading to direct organic impact (e.g. nutritional impact of famines).</p> <p>Overall, this article is very promising and can indeed shape future research on cardiometabolic outcomes of disasters like the COVID-19 pandemic.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1: Dr. Koichiro Shiba, Harvard University T H Chan School of Public Health

Comments to the Author:

This study is a systematic review of existing literature documenting the link between disaster exposures and subsequent cardiometabolic health. Its focus on the life-course aspect (i.e., timing of exposure) is unique. Based on the review, the authors concluded that any type of disaster exposure is linked to poor cardiometabolic health. Although this is an important topic, the manuscript needs substantial revision as it does not clearly articulate the rationale for the study's aims as it stands. Also, the interpretation of the results is somewhat questionable. Here, I describe some of the specific concerns I have.

1. In the Introduction, the authors need to provide more background information with regards to the life-course perspective. They could discuss things like why the impacts of disasters may differ depending on the timing of the exposure, public health implications of reviewing existing evidence from this angle, etc. The current introduction does not give a compelling rationale for the research aim.

RESPONSE: As suggested, we have now included more background information regarding the life-course perspective, “, it is also biologically plausible that exposure to a disaster may lead to long-term or chronic outcomes that could arise many years later and this may be modified by the time of exposure across the life-course. Consistent with established models of life-course epidemiology there may be critical periods of exposure (e.g., during development in childhood), where exposure to a disaster substantially increases later life disease risk, or exposure to a disaster may contribute to a chain of risk or accumulation of risks across the life-course (9,10)” (Background; page 3; paragraph 2).

2. Throughout the manuscript, there seems to be too much emphasis on the ongoing pandemic. I do not think the current study is particularly relevant for the public health strategies for the COVID-19 pandemic. After all, only a few papers they found focused on pandemic and none of them were about the COVID-19 pandemic. Nevertheless, the authors are making strong claims that the findings can inform policies related to COVID-19. For example, the authors wrote the following:

"the findings may serve to guide our understanding of expected outcomes and to develop future research to study the effects of COVID-19 on cardiometabolic outcomes. The results from this study can also be used to better understand the trade-off between the implementation of public health measures, such as physical distancing to reduce transmission of a virus, and the implications with access to healthcare, as the review found access to healthcare was limited following a disaster". It was not clear to me which result from this study supports this kind of claim.

RESPONSE: Thank you for this suggestion. We have now removed emphasis on the COVID-19 pandemic throughout the manuscript and more broadly focused all disaster types, and specifically removed that section from the discussion. Please see changes throughout the manuscript.

3. This study focused on the "long-term" effects of disasters on cardiometabolic health. This is an important point to emphasize because there is plenty of <https://jech.bmj.com/content/57/10/778> evidence documenting the short-term/acute effects of disasters as well. The authors briefly touched on this when they described their search strategy but stating their focus more clearly would enhance the readability of this paper.

RESPONSE: We have now provided more emphasis on this in the background, "Previous systematic reviews have focused on acute outcomes, specifically on the psychological impact of quarantine during pandemics (5), the impact on health outcomes after disasters in older adults (6), medically unexplained physical symptoms following disasters (7), and chronic medical interventions following a natural disaster (8). However, it is also biologically plausible that exposure to a disaster may lead to long-term or chronic outcomes that could arise many years later and this may be modified by the time of exposure across the life-course. Consistent with established models of life-course epidemiology there may be critical periods of exposure (e.g., during development in childhood), where exposure to a disaster substantially increases later life disease risk, or exposure to a disaster may contribute to a chain of risk or accumulation of risks across the life-course (9,10). There is currently no review on the long-term impacts of disasters, or more specifically, epidemics and pandemics on cardiometabolic outcomes across the life-course." (Background; page 3; paragraph 2).

4. The reviews revealed that there are mixed findings regarding the associations between disasters and cardiometabolic health. Not all studies reported significant differences in the outcomes by levels of exposure to disasters. Yet, the tone in Discussion is that there was clear evidence that disasters are linked to deteriorated cardiometabolic health. They briefly mentioned potential reasons for the mixed findings (e.g., length of follow-up), but did not sufficiently discuss other explanations (e.g., the difference in disaster type, definitions of "disaster exposures", what comparison was being made).

RESPONSE: As suggested we have revised the interpretation of results and the discussion and now focus more on the heterogenous nature of the included studies, "First, the heterogeneity across studies restricted the ability to conduct a meta-analysis. Studies varied in terms of study design, reported measures of effect, the comparison group (e.g., some studies did not include a comparator group), length of follow-up, timing and measurement of exposure, and primary outcomes and how they were measured. These differences in addition to the lack of statistical significance across studies make it difficult to draw overall conclusions." (Discussion; page 13; paragraph 1).

5. More discussion on study limitations is needed.

RESPONSE: As suggested we have now included a paragraph outlining limitations of the paper, “Although this review had several strengths, interpretation of findings should be done with caution due to limitations. First, the heterogeneity across studies restricted the ability to conduct a meta-analysis. Studies varied in terms of study design, reported measures of effect, the comparison group (e.g., some studies did not include a comparator group), length of follow-up, timing and measurement of exposure, and primary outcomes and how they were measured. Given the multi-disciplinary nature of the identified studies, a wide range of analytic approaches were used, and measures of effect varied. These differences in addition to the lack of statistical significance across studies make it difficult to draw overall conclusions. Very few studies have evaluated the long-term impacts of pandemics and epidemics on cardiometabolic outcomes, identifying a current gap in the literature. This made it difficult to truly assess if exposure to disasters at sensitive periods of development had lasting effects much later in life. Studies also reported insufficient data on subgroups that were at increased risk of worse cardiometabolic health outcomes and interventions that were implemented to mitigate risk of cardiometabolic outcomes. In addition, results were not often explored by sex and gender, or did not apply an equity lens. It has been noted that those of different levels of socioeconomic status experience differential cardiometabolic outcomes (89,90). This signifies the importance of exploring associations between exposure to disasters and cardiometabolic outcomes stratified by these factors. Understanding how these associations differ will also help to identify groups of people who will experience worse outcomes following a disaster.” (Discussion; page 13; paragraph 1)

Reviewer: 2: Dr. George Bazoukis, Geniko Nosokomeio Athenon o Euangelismos

#### Comments to the Author:

The authors presented a systematic review to determine the impact of disasters, including pandemics, on cardiometabolic outcomes across the life-course. It is a well written study reported the conflicting results of the different studies, However, while a meta-analysis would be helpful, the heterogeneity of the data reported makes the quantitative synthesis not feasible.

#### Comments:

1. In the study selection, data extraction section and critical appraisal sections, you mention that two independent reviewers and abstractors worked but you report several names. It is not clear what was the contribution of the authors or the way that the authors worked on this task.

RESPONSE: We have now clarified this in both the data extraction and critical appraisal sections, with the following “Studies were screened at title and abstract-level, and then at full-text by any two of the following independent reviewers VD, JL, MSA, YYM, ATA, ES, SI, JDM, RR LNA.” (Methods; page 5; paragraph 1), “Data were then extracted from all studies by any two of the following independent abstractors VD, JL, SMA, YYM, ATA, RR, ES” (Methods; page 5; paragraph 2) and “All studies were critically appraised independently by any two of the following individuals VD, JL, MA, YYM, ATA, ES, SI” (Methods; page 5; paragraph 3).

2. Table 1 can be included as a supplementary file and not in the main text.

RESPONSE: Thank you for this feedback, we will leave this up to the discretion of the Editor to decide where Table 1 will fit best.

3. In the table 3, it must be clear that the effect estimated in the last column are associated with the numbers of the outcomes in the previous column.

RESPONSE: A footnote has been added to Tables 3 and 4 stating, “Results are numbered to correspond with the numbered outcomes in the outcomes column” to improve clarity (Tables 3 and 4

pages 17-65).

4. A limitations section is required following the discussion section according to PRISMA statement.

RESPONSE: As suggested, a limitation section has now been added to the discussion in accordance with the PRISMA statement, “Although this review had several strengths, interpretation of findings should be done with caution due to limitations. First, the heterogeneity across studies restricted the ability to conduct a meta-analysis. Studies varied in terms of study design, reported measures of effect, the comparison group (e.g., some studies did not include a comparator group), length of follow-up, timing and measurement of exposure, and primary outcomes and how they were measured. Given the multi-disciplinary nature of the identified studies, a wide range of analytic approaches were used, and measures of effect varied. These differences in addition to the lack of statistical significance across studies make it difficult to draw overall conclusions. Many of the studies used a retrospective cohort study design and relied on administrative data sources as such many studies were unable to comprehensively adjust for confounders, including social determinants of health. Measurement error and misclassification of exposure status is also possible since many studies did not objectively measure disaster exposure or degree of impact, and instead used proxy measures of disaster exposure based on time and geography.” (Discussion; page 13; paragraph 1)

Reviewer: 3 Dr. Jawahar Mehta, UAMS

Comments to the Author:

An interesting article. In my opinion, the greatest strength of the article is the concept and timeliness of the study. Another strength is the in-depth and transparent description of the research methodology.

1. Some weaknesses of the study are the heterogeneity of the population, which is well addressed by the organization of results by natural vs man-made and adult vs childhood exposures. While the results could not be compared between studies due to the heterogeneity, it would be interesting to see similar studies which have similar exposures and populations compared.

RESPONSE: We have now further broken up the results to qualitatively summarize studies that evaluated perinatal/childhood exposures and perinatal/childhood outcomes, and perinatal/childhood exposures and adulthood outcomes in both the results (pages 6-10) and Table 3 (page 17). We have also further explained the results for studies that reported adult exposures (Results; pages 8-10).

2. I would further recommend fragmentation of the paragraphs in the results section so dissimilar observations can be separated to aid the flow of reading.

RESPONSE: As suggested, we have now broken up the results section text into smaller paragraphs (Results; pages 6-10).

3. I would also recommend a more detailed postulation of possible mechanisms in the discussion. Furthermore, is there a difference between outcomes of exposures related to the neurobiological axis (e.g., greater stress) and exposures leading to direct organic impact (e.g. nutritional impact of famines).

RESPONSE: We have now further developed our discussion on the potential mechanisms in which disaster exposure may lead to cardiometabolic outcomes. This can be found in the discussion in paragraphs titled “Biologic mechanisms (Discussion; page 11; paragraph 2) and “Unanswered questions and future research” (Discussion; pages 14; paragraph 1).

4. Overall, this article is very promising and can indeed shape future research on cardiometabolic

outcomes of disasters like the COVID-19 pandemic.

RESPONSE: Thank you for this feedback.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Bazoukis, George Geniko Nosokomeio Athenon o Euangelismos
<b>REVIEW RETURNED</b>	09-Mar-2021

<b>GENERAL COMMENTS</b>	The authors addressed adequately my comments
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<b>REVIEWER</b>	Mehta, Jawahar UAMS, Cardiology
<b>REVIEW RETURNED</b>	10-Mar-2021

<b>GENERAL COMMENTS</b>	The reviewer completed the relevant checklist but made no further comments.
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