PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Characterization of internal tremors and vibration symptoms among people with post-acute sequelae of SARS-CoV-2: A narrative analysis of Email and social media comments in a patient advocacy group
AUTHORS	Massey, Dorothy; Sawano, Mitsuaki; Baker, Anna; Güthe, Diana; Güthe, Nick; Shidlovsky, Suzanne; Fisher, Liza; Grady, Connor B; Caraballo-Cordovez, Cesar; Zhou, Tianna; Sharma, Richa; Krumholz, Harla

VERSION 1 – REVIEW

REVIEWER	Tsivgoulis, Georgios University of Athens, School of Medicine, Athens, Greece
REVIEW RETURNED	08-Aug-2023

GENERAL COMMENTS	The authors have adequately responded to all previous concerns raised in the first round of review. No further comments exist on my behalf.

REVIEWER	Anunciação, Luis Pontifical Catholic University Brazil
REVIEW RETURNED	16-Aug-2023

GENERAL COMMENTS	First of all, I would like to congratulate the authors for their work, which is extremely relevant to understanding the long-term COVID experience and the well-being of individuals. The work was written with objective language, and care was taken in the presentation and transparency of the collected data. Below are my suggestions for the manuscript: Abstract "We used common coding techniques for qualitative data synthesis and the constant comparative method of qualitative data analysis to categorize emails." I believe it is important to highlight the specific methods used, like what software was used. "This study describes key themes and experiences among a group of people reporting long COVID and having a prolonged and debilitating symptom complex that prominently features internal tremors and vibrations."It's important to highlight the importance of this findings in the literature. Introduction

| | "Post-Acute Sequelae of SARS-CoV-2 infection (PASC), also known as long Covid, is a condition that is marked by protean manifestation that varies considerably among individuals. (p.8). In the literature, the term long covid is used for several symptoms, so I think it is important to highlight the difference in the use of terms, the reason for using PASC, and to highlight what the main symptoms are right after.

"Proper clustering may enable efforts to identify biological signatures that help elucidate underlying mechanisms to guide the development of diagnostic and therapeutic strategies." (p.8). I recommend specifying why this technique helps, and also as highlighted in the previous comment, I believe that the term long covid is used at different levels of damage, therefore, I believe it is important to extend or present a little the reason for the biological cut, but presenting the extension cognitive and behavioral for example.

In general, I recommend that the authors extend the introduction (2 or 3 paragraphs), presenting in more detail about the experience of the long-term covid and its effects on the daily lives of patients, before presenting exclusively about the tremors.

Methods

Again, I congratulate the authors for the work's initiative, and I believe it was very important for them to add about the inspiration of the article. Regarding this section, I would only recommend adding about ethical aspects; even when it comes to contact via social networks, did the participants receive any consent terms? Was such a document presented at all stages?

Regarding data analysis, the processes were presented adequately.

Results

The results were presented in an adequate and objective way.

Discussion

The authors address mental health topics within the obtained clusters, however, I believe it would be important to discuss these findings with other previous works in the literature.

Based on these details, I believe that a new revision of the manuscript, with minor changes, would be important. |
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Georgios Tsivgoulis, University of Athens, School of Medicine, Athens, Greece Comments to the

Author:

8. This is a very interesting paper giving information of high interest. Although, it is difficult to

understand the number of participants included in this study, the exclusion number, and the total answers. This information should be described in the results area.

Response: Dr. Tsivgoulis, we appreciate your comment and have added the number of participants in this study in the Abstract and Methods sections.

Abstract

Setting and Design: A narrative analysis was performed on 140 emails and 450 social media comments from 140 individuals collected as a response to call for people to > 180,000 individuals participating in the Survivor Corps between July 15, 2021, and July 27, 2021.

Data Collection

Data were collected from unstructured responses that included 140 emails and 450 Facebook comments that occurred in response to Survivor Corps' calls for information in July 2021. Exact dates and names were removed and replaced with month and year and five-year age brackets to protect anonymity.

Survivor Corps collected data for this study in three steps. First, on June 27, 2021, the Survivor Corps founder, Diana Berrent Güthe, posted a Facebook poll, titled "Vibration/Buzzing/Pain Poll," in the Survivor Corps Facebook group. Responses were in a multiple-choice answer format, where respondents could also select multiple answers and add their own answer choices. There were 20 answer choices, each a statement relevant to vibration, tingling, buzzing, and neuropathic sensations (Supplemental Table 1). The research team included all poll responses as of July 16, 2021, which totaled 769. In addition, there were 162 Facebook comments posted by group members below the poll as of July 16, 2021, which were all included in data analysis.

Next, Survivor Corps member Nick Güthe posted in the Survivor Corps Facebook group on July 14, 2021, requesting that anyone with long Covid in the Facebook group who had experienced

"tremors or internal vibrations" and was interested in participating in a study comment below his post (Supplemental Figure 1). By July 16, 2021, there were 288 comments from group members in response to Nick Güthe's post, all of which were included in data analysis for this study. In response to members' comments, Nick Güthe and Diana Berrent Güthe requested that commenters share their story of these symptoms via email to Survivor Corps for the purposes of the study.

Finally, the Survivor Corps newsletter in July, 2021 also included a request for "Long Haulers" with "Neurological tremors or internal vibrations" to send details of their symptoms to Survivor Corps via email for this study (Supplement 1). Survivor Corps received 140 emails for this study between July 15, 2021 and July 27, 2021. All emails were included in data analysis. Including the Facebook comments from the initial poll and the comments from Nick Güthe's post, 450 Facebook comments were included in data analysis for this study.

Reviewer 2: Dr. Luis Anunciação, Pontifical Catholic University Brazil

Comments to the Author

1. The sample size is too small, the data is unstructured, and the information of the data analysis needs to be clarified.

Response: Dr. Anunciação, we appreciate your consideration and have added the number of participants in this study as follows in the Abstract and Methods sections.

Abstract

Setting and Design: A narrative analysis was performed on 140 emails and 450 social media comments from 140 individuals collected as a response to call for people to > 180,000 individuals participating in the Survivor Corps between July 15, 2021, and July 27, 2021.

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Supplemental Figure 1. Data Collection Process
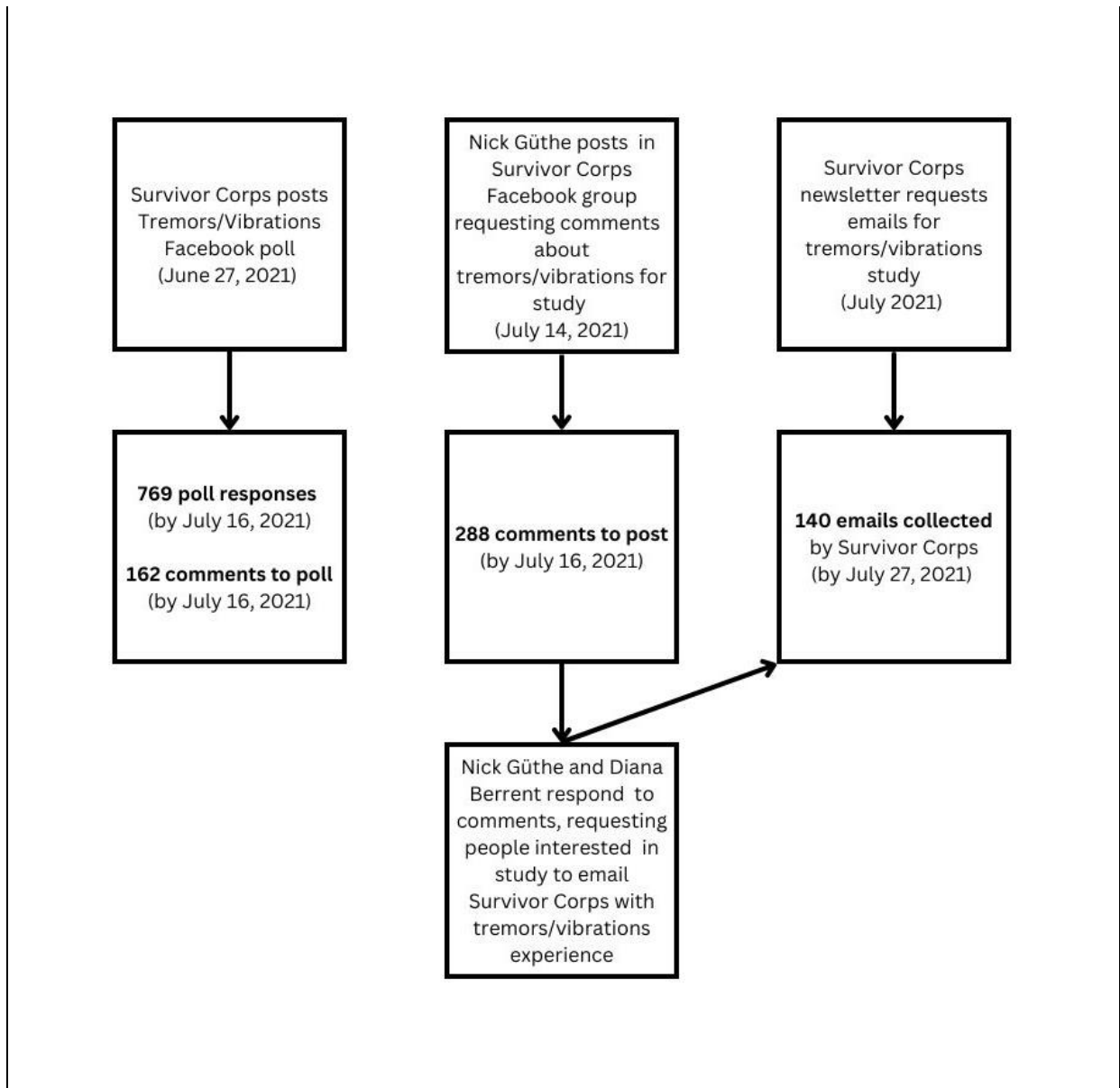
2. Just informing that R was used is not enough.

Response: Dr. Anunciação, thank you for your remark. We added description to the Methods, data analysis section, and Supplement 2. World Cloud Analysis Methodology, Supplement 3. Email Initial Code List.

Methods

Data Analysis

We used Word Cloud methodology to visualize the prevalence of terms. A Word Cloud is a visual representation of word frequency derived from written text. The more often the word appears within the passage being analyzed, the larger it appears in the image generated. We set the minimum frequency of words to be included in the Word Cloud to 3, the maximum number of words to 200, and removed extraneous filler words. All Word Clouds were generated using the quanteda, wordcloud, and tm packages in R v4.0.3 (R Development Core Team, Vienna, Austria).

Supplement 2. World Cloud Analysis Methodology

Leveraging the "quanteda" [1], "wordcloud" [2], and "tm" [3] packages in R, we constructed a Word Cloud of the most frequent words used to express some long-term effects of experiencing a COVID-19 infection among a Facebook COVID-19 survivors page. The data was converted from an xlsx to a txt file where it was then loaded as a corpus file, a specific type of file format required for Word Cloud generation, using the "Corpus" function in the "quanteda" package. To clean the corpus file, we utilized the "tm_map" function in the "tm" package to convert all text to lower case, to remove numbers, to remove punctuation and special characters, and then to collapse extra white space characters to a single blank space. Once cleaned, we built a term-document matrix which was then read into the "wordcloud" function within the "wordcloud" package. We set the minimum frequency of words to be included into the Word Cloud to 3, the maximum number of words allowed into the Word Cloud to 200, and then removed all extraneous, filler words such as "and", "comment", "view", "you." We included all adjectives, nouns, and verbs associated with COVID signs, symptoms, and experiences into the Word Cloud.

Supplement 3. Email Initial Code List

Below is listed the initial code list created by authors HMK and DM, prior to input from all team members and creation of the final code.

1) Symptom Perception and Location

Vibrations and tremors were described concomitantly, with descriptions of internal vibrations, visible tremors, and some people experiencing both.

Vibration or tremor site varied, from the entire body to localization in extremities, chest, abdomen, and other locations.

Vibrations and tremors occurred with other symptoms of varying number.

Vibrations and tremors could cause severe pain.

2) Initial Symptom Onset

Vibration and tremor initial onset varied, from the day of initial infection to weeks later.

Vibrations and tremors occurred following or during acute COVID-19 infections that varied from mild to severe.

3) Symptom Timing

Vibration and tremor episodes could be brief, or could be prolonged, even constant.

Vibration and tremor episodes could occur constantly, daily, or only when relapses occurred.

People experienced vibrations and tremors over different time periods (even if they were episodic), and some did not have improvement in symptoms after more than a year.

4) Symptom triggers or alleviators

The vaccine was associated with both improvement in symptoms for some people, and a relapse in symptoms for others.

Exercise and activity were associated with onsets of tremors and vibrations.

A variety of self-treatment strategies, such as diet modifications and humming, were used to alleviate tremors and vibrations.

5) Change from Baseline Health Status

People with vibrations and tremors had varying health states before their COVID-19 infection, from those who were completely health to those with pre-existing conditions.

6) Experience with Medical Establishment

Medical testing failed to reveal the mechanism of either tremors or vibrations.

Tremor and vibration symptoms were sometimes doubted or dismissed by doctors.

Medications have been provided for tremor symptoms, with varying results.

7) Effect on People's Lives and Livelihood

Vibrations and tremors were associated with mental health effects, ranging from anxiety to suicidal thoughts.

Vibration and tremor symptoms could cause disability people.

Vibration and tremor symptoms could cause financial stress, through a combination of medical care costs and loss of income from medical leave.

Vibrations and tremors could disturb or prevent sleep.

Vibration and tremor symptoms could prevent people from working or carrying out daily life activities.

3. The information of the seven domains is hard to follow and understand, and the way these domains were formed is absent.

Response: Dr. Anunciação, thank you for your comment. We added description to the Methods, Data

Analysis section as follows.

Methods

Data Analysis

<u>Emails</u>

Email data were analyzed using common coding techniques for qualitative data and the constant comparative method of qualitative data analysis.[18] Coding of the data was accomplished in iterative steps. An initial code list was generated after an initial evaluation of the data by research team members (HMK and DM) (Supplement 3). The initial code list was created in three steps. First, each reviewer separately read the 140 emails (with names and exact dates redacted). Next, each reviewer separately read the 140 emails while creating themes based on the contents of each email, until each statement about internal tremors or vibrations in every email had been assigned to a theme. The reviewers then met to discuss shared themes and reached a consensus on the list of themes. The reviewers then grouped the themes into 7 larger domains. At this point, the full research team reviewed the code structure, including a study participant (LF), for logic and breadth.

4. The conclusion that states that "a group of people who report experiencing PASC exhibit a prolonged and debilitating symptom complex that prominently involves vibrations and tremors" is not highly correlated with the data collection and data analysis.

Response: Dr. Anunciação, thank you for your concern. We agree that our findings do not fully support the conclusion and have changed to the following description.

Abstract

Conclusions: This study describes key themes and experiences among a group of people reporting long COVID and having a prolonged and debilitating symptom complex that prominently involves internal tremors and vibrations.

Conclusion

In conclusion, some people report experiencing internal vibration and tremor symptoms, often causing intense suffering, after a self-reported history of SARS-CoV-2 infection. The symptoms had some common features but there was variability in timing, concomitant symptoms, and impact. Further research is needed to understand and alleviate this suffering, by studying the extent and scope of these symptoms, possible mechanisms, and potential treatment.

5. The authors don't discuss the limitation of the study. They just list some issues without clarifying what was done to fix them.

Response: Dr. Anunciação, thank you for your concern. We have added the study limitation in the last paragraph of the Discussion section, accordingly.

Discussion

This study has limitations. This Facebook group was a convenience sample and no information about their characteristics or how many of them have had a laboratory-confirmed case of infection with SARS-CoV-2 are available. Any information about testing is based on self-report. As such, we cannot determine whether these symptoms were caused by their infection with SARS-CoV-2, nor whether the symptoms reported by different people were the same symptom complex or of the same etiology. There was little demographic information provided, so we also cannot determine whether the sample is representative of the population experiencing these symptoms. The data are self-reported from people in response to a query. The information was limited to what people provided and there was no follow-up to obtain more information. The study presents what people shared on

their initial communication. This limited the scope of findings and may have excluded information that medical professionals would have found relevant. This also may indicate that our sample was biased in that people had to be healthy enough to be active members of a patient community (Survivor Corps) and to email a response to the group. People could have also been more likely to be suffering greatly as they had to have the motivation to be in a long Covid patient group and to respond to the query. Finally, because this is a convenience sample of people responding to the queries, this study cannot provide information on the incidence and prevalence of these symptoms.