PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Distress and resilience of healthcare professionals during the COVID-19 pandemic (DARVID): study protocol for a mixed-methods research project
AUTHORS	Fuchs, Alexander; Abegglen, Sandra; Berger-Estilita, Joana; Greif, Robert; Eigenmann, Helen

VERSION 1 – REVIEW

REVIEWER	Alison Scope The University of Sheffield UK
REVIEW RETURNED	13-May-2020

GENERAL COMMENTS	This study protocol describes mixed methods research investigating distress and resilience of healthcare professionals during the COVID-19 pandemic. The introduction presents a strong justification for the study and in addition to looking at distress interestingly looks at 'post-traumatic growth' and psychological resilience, which is a strength of the proposed research. In general the methods, measures and analysis are clearly described and appear to be appropriate. I have just a few minor points for clarity. It was not clear how appropriate participants will be identified. On Page 7, line 165-166, it is stated that 'The survey link will be primarily distributed through social media (LinkedIn, Facebook, Twitter, WhatsApp, Threema), using the 'snowballing' sampling technique'. Will this be via routes limited to HCPs and how will eligibility be verified. Further, on P7 line 172 - 174. The participant inclusion and exclusion criteria, state that the authors will include HCPs over 18 years of age who agree to participate, what definition of a HCP is being applied here or is this self defined? Some further detail on this would be useful here. This will also have implications for the analysis. P7, line 177-180. I found this paragraph a little confusing, although I think this is just due to a little repetition which can be easily resolved with some editing.

REVIEWER	Yvonne Bombard; Chloe Mighton assisted with this review University of Toronto, Canada
REVIEW RETURNED	16-May-2020

GENERAL COMMENTS	Thank you for the opportunity to review this paper that reports the protocol for a timely study. There are several ways the authors may consider improving the rigor of the paper.

	MAJOR POINTS Methods The authors should state whether qualitative and quantitative methods will be given equal priority, or which one will be prioritized. The authors should provide more details about how quantitative and qualitative strands of their study will be integrated, and details about how they intend to triangulate quantitative and qualitative findings. The authors should provide methodological references to support their mixed methods study design, as currently none are provided. The author should provide details about the quantitative instruments used, if available, such as reliability indices of the surveys. The authors should also provide details about whether they pilot tested their questionnaire. The authors state, “Purposive sampling into homogeneous groups will be performed, according to patient availability.” (Line 240) The authors should state what characteristics they using to select participants for their sample, and how they are defining homogeneity of the groups. The authors also should describe the purpose of the homogeneous groups. Are they intending to conduct focus groups, or one-on-one interviews? The authors should comment on threats to the internal validity of the quantitative study design and how they plan to mitigate bias. For instance, surveys administered at multiple timepoints to the same group are susceptible to attrition and multiple testing bias. The authors should also comment on strategies that they will employ to ensure rigor of the qualitative component of their study. MINOR POINTS Strengths and limitations The authors state, “the participating healthcare professionals will consent and electronically disclose their emails […].” This does not need to be highlighted as a key strength or limitation of the study. The authors state, “The survey will be accessible only in English, which might influence the compliance of non-English native speakers.” (Lines 66-67) The authors should briefly elaborate how this could impact the validity of their findings. Introduction Line 72: The authors state, “SARS CoV-2 causes severe hypoxaemic pneumonia […]” It may be more accurate to state, “SARS CoV-2 causes coronavirus disease (COVID-19).” Methods The authors should provide more detail about how they developed their interview guide.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1, Dr. Alison Scope

Comment 1: It was not clear how appropriate participants will be identified. On Page 7, line 165-166, it is stated that 'The survey link will be primarily distributed through social media (LinkedIn, Facebook, Twitter, WhatsApp, Threema), using the 'snowballing' sampling technique'. Will this be via routes limited to HCPs and how will eligibility be verified.

Our reply: We thank the reviewer for this comment. This way of distribution is not limited to HCPs as we did not invite single HCPs by a unique personalized link. We decided for the « snowballing recruitment » because it allows for a high exposure and participation in a very short recruiting time period. Therefore, the survey link was sent to HCP organizations to be forwarded to their members, to individual lists of HCPs from the study group members, and via social media contacts within HCP. We cannot assure that non-HCP got the invitation but from the informed consent and the instructions of the survey it was clear that we address HCPs. We rely on participants' self-declaration of their professional role. We addressed HCPs personally in our invitation letter and participants must confirm before starting in the survey that they are HCPs, together with their informed consent. (SDC 1 / Online questionnaire Page 1, Line 17). Later in the survey participants have to specify their health profession, which will provide us with more details (SDC 1 / Online questionnaire Page 4, Line 3-16). We have introduced the following sentence to clarify this (Page 7, Line 179-180): "(…) we contacted several healthcare professional associations and societies in different countries to ensure an HCP-oriented distribution of the survey (…)"

Comment 2: Further, on P7 line 172 - 174. The participant inclusion and exclusion criteria, state that the authors will include HCPs over 18 years of age who agree to participate, what definition of a HCP is being applied here or is this self defined? Some further detail on this would be useful here. This will also have implications for the analysis.

Our reply: Thank you for the comment. We added a definition of HCP according to the International Labour Organization for clarification. It now reads (Page 7-8, Line 185-190): "A HCP is defined as a postgraduate person listed in the sub-major group 22 (Health Professionals), according to the International Standard Classification of Occupations (ISCO-08), with exclusion of minor group 225 (Veterinarians). This includes medical doctors, nursing and midwifery professionals, traditional and complementary medicine professionals, paramedical practitioners, dentists, pharmacists and environmental and occupational health and hygiene professionals."

Comment 3: P7, line 177-180. I found this paragraph a little confusing, although I think this is just due to a little repetition which can be easily resolved with some editing.

Our reply: We would like to thank the reviewer for mentioning this. We edited the paragraph for clarity and it now reads (Page 8, Line 194-196): "The primary outcome of this study is the variation in COVID-19 anxiety in different regions, over three time periods, measured using a modified version of the Swine Flu Anxiety Items [SFI])33 a 10-item survey developed to measure anxiety disorders and somatization (Cronbach's alpha = 0.85)."

Reviewer #2, Dr. Yvonne Bombard assisted by Chloe Mighton

Comment 1: The authors should state whether qualitative and quantitative methods will be given equal priority, or which one will be prioritized.

Our reply: Thank you. We have introduced in the “Study design overview” section of the manuscript the following sentence (Page 7, Line 158-159): “Data collection will be sequential (first quantitative and then qualitative) but both study parts will be given equal priority.”

Comment 2: The authors should provide more details about how quantitative and qualitative strands of their study will be integrated, and details about how they intend to triangulate quantitative and qualitative findings.

Our reply: Thank you. We have rephrased the “Study design overview” section of the manuscript and now reads “We will conduct a sequential mixed-methods study based on an explanatory design” (Page 6, Line 145).
We added the following details to clarify that point: “The quantitative data and their subsequent analysis will provide a general understanding of the development of mental health symptoms during the pandemic, while the qualitative data and their analysis will refine and explain the statistical findings in more depth, by exploring participants´ views, thoughts and feelings.” (Page 6-7, Line 155-158)

Comment 3: The authors should provide methodological references to support their mixed methods study design, as currently none are provided.

Our reply: Thank you. We have introduced the following references to support the mixed methodology (Page 6, Line 145 and Page 7 Line 158):
• Ref. 26. Schifferdecker KE, Reed VA. Using mixed methods research in medical education: basic guidelines for researchers. Med Educ 2009;43(7):637–44. doi: 10.1111/j.1365-2923.2009.03386.x
• Ref. 27. Rossman GB, Wilson BL. Numbers and words: Combining quantitative and qualitative methods in a single large-scale evaluation study. Evaluation review 1985;9(5):627-43.
• Ref. 28. Tashakkori A, Teddlie C, Teddlie CB. Mixed methodology: Combining qualitative and quantitative approaches: Sage 1998.
• Ref. 29. Creswell J. Research Design: Qualitative, Quantitative and Mixed Methods Approaches. 4 ed. Thousand Oaks, CA.: SAGE 2014.

Comment 4: The author should provide details about the quantitative instruments used, if available, such as reliability indices of the surveys. The authors should also provide details about whether they pilot tested their questionnaire.

Our reply: Thank you for this valuable comment. We added the corresponding Cronbach's alpha for internal reliability to each of the used validated instruments. (Page 8, Line 196-208).
Except for the demographic questions and the two self-created items, all of the used instruments have been already validated and were published previously. We did not see the need for testing of their reliability again. Nevertheless, pilot testing of the final survey for face validity was performed by the co-authors and some of the authors` colleagues. Since the pandemic was in an exponential grow period and such data acquisition needed to be done immediately, a broader pilot testing was not feasible. As all of us we were not aware of the upcoming pandemic, a previous planning of that survey was virtually impossible. We added the following sentence: “We undertook a short pilot testing with the co-authors and some of the authors` colleagues”. (Page 7, Line 181-182)

Comment 5: The authors state, “Purposive sampling into homogeneous groups will be performed, according to patient availability.” (Line 240). The authors should state what characteristics they using to select participants for their sample, and how they are defining homogeneity of the groups. The authors also should describe the purpose of the homogeneous groups. Are they intending to conduct focus groups, or one-on-one interviews?

Our reply: Thank you for this remark. We have introduced the following statement to better define the characteristics and purpose of the homogenous groups. You can now read (Page 10, line 260-263) “As the study is sequential in nature, it is impossible to pre-emptively select participants for the qualitative phase. Therefore, we will perform stratified purposive sampling into homogeneous focus groups, stratified by front- or second-liners, profession and country of origin, to enable comparisons.”. We included the corresponding citations that fundament our choice.

Comment 6: The authors should comment on threats to the internal validity of the quantitative study design and how they plan to mitigate bias. For instance, surveys administered at multiple timepoints to the same group are susceptible to attrition and multiple testing bias.

Our reply: Thank you for this important remark. One possible treat on the study’s internal validity is attrition. From a methodological view point, we applied oversampling technique to minimise the possible bias of unit nonresponse. We calculated with a drop-out rate of 33% per country group in our sample size analysis. Attrition of one-third in a study period of nine months is comparable to other longitudinal studies in the field of medical research:

• Booker, C. L., Harding, S., & Benzeval, M. (2011). A systematic review of the effect of retention methods in population-based cohort studies. BMC public health, 11(1), 249;

• Gustavson, K., von Soest, T., Karevold, E., & Røysamb, E. (2012). Attrition and generalizability in longitudinal studies: findings from a 15-year population-based study and a Monte Carlo simulation study. BMC public health, 12(1), 918,

• Mihara, S., & Higuchi, S. (2017). Cross-sectional and longitudinal epidemiological studies of Internet gaming disorder: A systematic review of the literature. Psychiatry and clinical neurosciences, 71:425-44.

To prevent a high attrition we will foster the communication between study coordinators and participants, we will send several personalized follow-up invitations, we invested time in an optimal design and an adequate length of the questionnaire.

From a statistical point of view, we will apply different methods in accordance with the unravelled missing value patterns. If the missing data mechanism is MAR/MCAR (missing at random, missing completely at random), we will apply hierarchical linear modelling with maximum-likelihood estimation, which models all available observations with no attempt to impute missing values. This method will provide unbiased estimates in the presence of missing observations under the less restrictive assumption “missing at random”. Likelihood-based, mixed-effects analyses have been shown to outperform traditional approaches with substantial missing values (e.g., ANCOVA with last observation carried forward) in terms of the magnitude of bias on effects and standard errors. Moreover, multilevel models perform partial pooling (shifting estimates toward each other), whereas classical procedures typically keep the centers of intervals stationary, adjusting for multiple comparisons by making the intervals wider In case of MNAR-missing data patterns (missing not at random), we will perform multilevel multiple imputation according to the joint modelling paradigm and impute all incomplete variables simultaneously with the mitml-package in R Statistical Language (50’000 iterations (burn-in), with 10’000 imputations every 100 iterations).

A second concern is multiple testing bias. We agree with this important concern, especially in theory-driven hypothesis testing approaches. As COVID-19 is a new potential burden for HCP and currently there is only a few researches on the development of COVID-19 anxiety, our study is exploratory in

nature. Therefore, we did not state specific hypotheses. Our aim is to shed light on the optimal number of predictors without significantly reducing the R2 coefficient of the model on COVID-19-anxiety over time. Thus, we will apply stepwise and simultaneous hierarchical regression and we will not draw any causal inference from our results.
Finally, a third possible threat is self-selection of our participants. We use a non-probability sampling approach (i.e. snowballing) as we want to target a broad participation of international HCP. We connected with several associations to ensure a wide range of survey distribution. From a statistical view point, we will analyse the differences between participants' key characteristics and HCP population characteristics in the respective countries to detect any sample selection bias.

To address the potential threats on internal validity of the studies from a methodological view point, we included the following paragraph in the data collection section (Page 7, Line 177 - 181): "To minimize the possibility of attrition bias we ensure a good communication between study coordinators and participants, send several personalized follow-up invitations, and apply oversampling technique. Moreover, we contacted several healthcare professional associations and societies in different countries to ensure an HCP-oriented distribution of the survey and to minimize sample selectivity bias."

To address the potential threats on internal validity from a statistical view point, we included the following paraph in the Statistical Analysis Plan section (Page 10, Line 248 - 252): "Statistical strategies for dealing with threats to internal validity (i.e. attrition bias, sample selectivity bias , multiple-testing bias) include extensive drop-out analyses, reporting of attrition by socioeconomic factors, statistical comparison of participants key characteristics with population characteristics, and applying of linear hierarchical regression analyses, which include all available data and compensate for multiple testing."

Comment 7: The authors should also comment on strategies that they will employ to ensure rigor of the qualitative component of their study.

Our reply: Thank you for your comment. We have introduced in the "Qualitative Phase" description section a paragraph to describe our strategies to ensure rigour. You can now read (Page 10-11, Line 275-278) "Strategies for dealing with threats to validity of the qualitative data used in this study include method triangulation, member-checking (also known as participant validation), peer support and an audit trail. The use of triangulation of different data sources will enhance objectivity and strengthen intersubjective agreement. A thorough methodologic description will also help credibility".

Comment 8: The authors state, "the participating healthcare professionals will consent and electronically disclose their emails […]." This does not need to be highlighted as a key strength or limitation of the study.

Our reply: We thank the reviewer for mentioning this and have deleted the aforementioned part of the sentence from the manuscript. It reads now: "The participating healthcare professionals might not be representative of the entire population and for all countries" (Page 3, Line 64-65)

Comment 9: The authors state, "The survey will be accessible only in English, which might influence the compliance of non-English native speakers." (Lines 66-67) The authors should briefly elaborate how this could impact the validity of their findings.

Our reply: Thank you for your comment. We are aware of this language bias, but in an international

survey this is the only way to guarantee a single version of the questionnaire. Translation of the questions and the previously validated questionnaires into a variety of languages was beyond the available human and time resources of the study group. Therefore, we edited the sentence (Page 3, Line 66-68), which now reads: “The survey will be accessible in English, to target a broad participation of international HCPs. This may limit participation and compliance of HCPs in regions where English is not common and introduce biases due to underrepresentation or misunderstandings.”

Comment 10: Line 72: The authors state, “SARS CoV-2 causes severe hypoxaemic pneumonia […]” It may be more accurate to state, “SARS CoV-2 causes coronavirus disease (COVID-19).”

Our reply: Thank you for this comment. We edited this statement to (Page 4, Line 72-74): “SARS CoV-2 causes coronavirus disease 2019 (COVID-19) which can lead to severe hypoxaemic pneumonia and other serious complications.”

Comment 11: The authors should provide more detail about how they developed their interview guide.

Our reply: Thank you for this comment. We have introduced the following sentence in the “Data collection” subsection of the qualitative phase description (Page 10, Line 269-273): “We used the protocol proposed by Castillo-Montoya to develop a semi-structured interview guide (Supplemental Digital Content 2). We first ensured that interview questions were aligned with our research questions, we then constructed an inquiry-based conversation, we asked for external feedback on interview protocols and we will pilot the interview guide in the near future.”

VERSION 2 – REVIEW

REVIEWER	Alison Scope The University of Sheffield, UK
REVIEW RETURNED	05-Jun-2020

GENERAL COMMENTS	Many thanks to the authors for providing a thorough revision of the paper. I am happy that my previous comments have been addressed appropriately.

REVIEWER	Dr Yvonne Bombard, assisted by Chloe Mighton Institute of Health Policy, Management and Evaluation, University of Toronto, Canada
REVIEW RETURNED	17-Jul-2020

GENERAL COMMENTS	Thank you for your thorough responses to the previous comments.