

Dear editor and reviewers:

Thank you for the opportunity to revise our original manuscript. We highly appreciate the returned suggestions on our manuscript. All comments were very uplifting and had immensely contributed to strengthening our manuscript. Find below our responses to your comments, one-by-one. All changes in the manuscript are highlighted in yellow. A native English speaker with extensive experience in scientific texts ([Julia Mortimer - English Language Services Worldwide](#)) edited and polished the written English of the final manuscript, making several rectifications of unclear portions.

Sincerely,

Authors

Marcos O. Carvalho-Alves, M.D.
Vitor A. Petrilli-Mazon, M.D.
André R. Brunoni, M.D., Ph.D.
André Malbergier, M.D., Ph.D.
Pedro Fukuti, M.D., PhD.
Guilherme V. Polanczyk, M.D., Ph.D.
Euripedes C. Miguel, M.D., Ph.D.
Felipe Corchs, M.D., Ph.D.
Yuan-Pang Wang, M.D., Ph.D.

Reviewer #1:

Q1: “Introduction and background: I need from the authors to give us more data about the other Hospitals in Brazil to compare between their Hospital and others in the same country”

R. Thank you for this comment. This point is important for comparing data in our Introduction because the present study is a single-center survey. Therefore, in this section, we included results from a Brazilian study conducted during the first wave of COVID-19 (Osório et al., 2021; 2022). They also found high rates of anxiety, depression, trauma, and insomnia. However, they showed lower rates of trauma than us, which may be since their analysis was not over the peak of the first wave, and they included professionals from different Brazilian institutions, not necessarily COVID-19 referral centers (Page 5, ln 142-145).

Regarding the Brazilian context, a study composed of Brazilian HCWs from different regions also found high rates of anxiety (43.3%), depression (40.2%), trauma (36%), and insomnia (61.5%) (Osório, 2021).

Reference:

Osório FL, Silveira ILM, Pereira-Lima K, Crippa JAS, Hallak JEC, Zuardi AW, Loureiro SR. Risk and Protective Factors for the Mental Health of Brazilian Healthcare Workers in the Frontline of COVID-19 Pandemic. *Front Psychiatry* 2021; **12**:662742 [PMID: 34393843 DOI: 10.3389/fpsyt.2021.662742]

Osório FL, Zuardi AW, Silveira ILM, Crippa JAS, Hallak JEC, Pereira-Lima K, Loureiro SR. Monitoring the mental health and professional overload of health workers in Brazil: a longitudinal study considering the first wave of the COVID-19 pandemic. *Front Psychiatry* 2022 [in press].

Q2: “In results section, the authors wrote in the 1st paragraph “most of”we must avoid these words in results illustration. We just write the percentage only”

R. Following your recommendation, we rewrote the 1st paragraph of our Results section, changing the expression “most of” to percentage values only. We hope that it is now appropriate (Page 13, In 363-365).

Considering **Table 1**, out of 1,000 participants who completed the survey, 83.9% were women, 34.3% were aged 30 to 40 years old, 57.4% were married or living with a partner, and 72.9% had an educational level of university graduate or higher.

Q3: “In methodology section: the authors have to explain more the site of medical staff like in ER, COVID-19 ICU, because this have a burden on the HCWs”

R. We agree this is an important point. We added more explanation about the site of the professionals in the methodology section (Page 7, In 196-199). Furthermore, We included the description in **Table 1**. Of all assessed professionals, 39.3% were actively working in high-risk sectors, such as Inpatient Ward, Intensive Care Unit, and Emergency Room. It is important to highlight that 79.6% of our sample reported direct contact with COVID-19 patients.

Participants

The inclusion criterion was that participants had to be working at the hospital, in person or from home, at the time of data collection. Medical doctors, nurses, nursing assistants, dentists, speech therapists, psychologists, occupational therapists, dieticians, physical therapists, social workers, pharmacists, clinical laboratory technicians, radiological technologists, and administrative professionals were included as HWs. Professionals from all hospital sites were invited, including the emergency room, inpatient wards, intensive care units, outpatient care, operating room, pharmacy, and laboratory. There were few exclusions as current workers were all adults and able to respond to an online questionnaire. Potential participants did not present linguistic problems, but limited access to the internet from a computer or mobile phone could have been an obstacle to participation.

Table 1: Socio-demographic and clinical characteristics of participants (n = 1000).

Characteristics	n (%)
Work sector	
Emergency Room	60 (6.0)
Inpatient Ward	176 (17.6)
Intensive Care Unit	157 (15.7)
Outpatient Care	128 (12.8)
Operating Room	44 (4.4)
Pharmacy	36 (3.6)
Laboratory	84 (8.4)
Other sectors	163 (16.3)

Q4: “In Discussion section: The authors have to explain more about the duration of the institutional support, it was just during the acute phase only because all of us know that we have now the concept of Chronic COVID-19 sequelae.”

R. This is a great suggestion. For the current study, we included only the evaluation of the institutional support during the peak of the first wave, which were cross-sectional data from the baseline of an ongoing longitudinal study. Data of institutional support in further phases of the pandemic were recorded and will be included in forthcoming analyses. Regarding “chronic COVID-19 sequelae”, we are aware that different neuropsychiatric COVID-19 sequels have been reported, such as Alzheimer's disease and anxiety disorder. We highlighted the importance of longitudinal study to capture this emerging concept in the following text of our discussion (Page 21, ln 385-387):

For the purposes of the present paper, we only evaluated the institutional support during the peak of the first wave in Brazil. However, several studies have demonstrated concerns about chronic COVID-19 sequelae, which could be associated with mental health outcomes among other clinical conditions, requiring specific treatments and continuous aid (Visco *et al.*, 2022; Tirozzi *et al.*, 2022).

Reference:

Visco V, Vitale C, Rispoli A, Izzo C, Virtuoso N, Ferruzzi GJ, Santopietro M, Melfi A, Rusciano MR, Maglio A, Di Pietro P, Carrizzo A, Galasso G, Vatrella A, Vecchione C, Ciccarelli M. Post-COVID-19 Syndrome: Involvement and Interactions between Respiratory, Cardiovascular and Nervous Systems. *J Clin Med* 2022; **11**:524 [PMID: 35159974 DOI: 10.3390/jcm11030524]
Tirozzi A, Santonastaso F, de Gaetano G, Iacoviello L, Gialluisi A. Does COVID-19 increase the risk of neuropsychiatric sequelae? Evidence from a mendelian randomization approach. *World J Psychiatry* 2022; **12**(3): 536-540. [DOI: 10.5498/wjp.v12.i3.536]

Reviewer #2:

Major comments: Authors describe observational data with regards to emotional stress in Brazilian population. Major comments: Total invites 22,056, final response 1377, included in analysis 1000 only. Very poor response rate. Not sure if the results from survey with a response rate of 4.5% is really representative to draw any meaningful conclusions Due to the low response rate, there is also a risk of selection and response bias. Not sure if authors can do anything about it but it should clearly be states as one of the limitations.

R. First of all, we appreciate your positive comments on the overall execution of the study. Your first rating of “General Acceptance” was really enthusiastic for our research team. Find below our answers to your concerns. Specifically, we rewrote the limitation section, echoing your concerns about the low response rate and the consequent risk of selection and response bias.

First, we would like to remark here that our observational study was not a strict prevalence study, thus the rate of each proportion should better be viewed as a descriptive frequency of symptoms, behaviors, or environmental conditions in our institution. Certainly, the data is not representative of our institutional healthcare workers nor should be generalized to other samples. External validity was not assured to other population samples. We have acknowledged this in Limitations.

Second, bearing in mind the non-representativeness of data, we have circumvented this limitation by conducting a factor analysis and subsequent regression analysis. For the factor analytic strategy, the major requirement is a high between-variable correlation and a large enough sample size to extract meaningful factors. In other words, the factorial model is a data reduction technique that is reliant on the internal structure of covariance, but not on data distribution or representativeness. Furthermore, linear regression analysis is an estimate of the likelihood of a dependent variable (factorial dimensions) to be predicted by independent variables (e.g., demographic characteristics and institutional support), which magnitude was expressed as a coefficient β . As such, a standardized β coefficient compares the strength of the effect of each individual independent variable to the dependent variable. Once again, this relationship is not affected by data representativeness, but the sample size could have an impact on the precision of the estimate. The model fitness of our analyses has indicated a good adjustment (R^2) with a fair 95% confidence interval (see Results). In this line, for example, we found that institutional support indicated the following salient associations with all dimensions of emotional distress: $\beta = -0.26$ (-0.33 to -0.18), $P < 0.001$; $\beta = -0.41$ (-0.48 to -0.33), $P < 0.001$; $\beta = -0.22$ (-0.28 to -0.13), $P < 0.001$, with an adjusted R^2 of 0.18, 0.29 and 0.09, respectively for dimension of avoidance/re-experience, depression/anxiety, and insomnia. Hence, we have to agree with you that there are a few things to fix the lack of sample representativeness, but we have carefully planned the analyses to present sound results (Page 21, ln 598-602).

First, although our sample size was large enough, it was not representative of our institutional HWs, with a low response rate of 4.5%, and might be vulnerable to self-selection and response bias. Nevertheless, a good fit factorial model does not require a representative sample, but a large enough size with correlated items (Hair, 2013).

Reference:

Hair JF, Black WC, Babin JB, Anderson RE. *Multivariate Data Analysis*. 7th. ed. United Kingdom: Pearson; 2013: 90-147.

Q1: Need more information about collinearity and confounding. Please provide VIFs for the test of collinearity. Results can be described in the main text with highlighting the salient findings without extensive details of statistical analysis (that could be included as a supplement).

R. This is a good suggestion. We have estimated and included the VIFs for the test of collinearity in the supplementary material. Moreover, we added all salient findings in the section of Statistical Analysis (Page 12, ln 338-341).

A collinearity analysis was subsequently conducted using the *polycor* package to rule out the correlation between independent variables. All analyzed variables had a Variance Inflation Factor (VIF) below 3 (for more details, see Supplementary material), suggesting that multicollinearity was not a problem in our data.

Supplementary material:

Table 1: Variance Inflation Factor (VIF) between independent variables

Independent variables	Variance Inflation Factor (VIF)
Age	1.07
Gender	
Female	Reference
Male	1.13
Occupation:	
Physicians	Reference
Nurses	2.75
Other healthcare workers	2.36
Administrative workers	2.21
Marital status	
Unmarried	Reference
Married	1.04
Educational level	
< University graduate	Reference
≥ University graduate	1.15

Direct contact with COVID-19 patient (hours per week)	1.5
Previous psychiatric or psychological treatment (self-reported)	1.05
Had COVID-19 (self-reported)	1.03
Close family or friend hospitalized or who died due to COVID-19	1.02
Ethical conflict	1.08
Personal motivation	1.81
Institutional support	1.82

Q2: With regards to running multiple models in the analysis, was there a Bonferroni adjustment for the P value? Needs to be explicitly mentioned in the text.

R. We would like to thank you again for this opportunity to improve our original study. Considering your suggestion, we included in our statistical analysis the Bonferroni test. The fitness of all three crude models was kept statistically significant ($P < 0.001$), and our main results and conclusions remained unchanged even after adjustment. Finally, we rewrote the results section, mentioning that we used the Bonferroni test for multiple models (Page 16, ln 441-442).

Predictors of the mental health dimensions

Table 4 shows crude and adjusted multiple linear regression models which were built to evaluate potential predictors for each of the emotional dimensions retained from the EFA. First, models were carried out using the following independent variables: direct contact with a COVID-19 patient, previous psychiatric and psychological treatment, had COVID-19, close family or friend hospitalized or died due to COVID-19, ethical conflict, personal motivation, and institutional support. The fitness of all three crude models was statistically significant ($P < 0.001$). Likewise, the adjusted R^2 for each of the models was 0.14, 0.25, and 0.08 respectively. Second, three final models were adjusted for age, gender, marital status, educational level, and occupation, yielding an adjusted R^2 of 0.18, 0.29, and 0.09, respectively. All adjusted models were statistically significant ($P < 0.001$) by *F*-test, considering the Bonferroni test for multiple models.

Q3: Was the past history of psychological/psychiatric treatment associated with higher rates of stress/depression or higher score on PHQ?

R. In our analysis, the history of psychological/psychiatric treatment was self-reported (we included this information in Tables 1 and 4). This variable was remarkably associated with high scores in all retained emotional dimensions. We reanalyzed our data through chi-squared tests for the history of psychological/psychiatric treatment and scores of each used scale, including PHQ-9, considering its cut-off points. We found that this variable was significantly associated ($p < 0.001$) with raw scores of all these scales. Therefore, pre-pandemic psychopathology was associated with higher rates of mental health outcomes (e.g., depression, anxiety, and stress) (Page 16, ln 450-453).

Moreover, the final sociodemographic adjusted models indicated that participants with previous psychiatric or psychological treatments presented a significant likelihood of manifesting the three mental health dimensions ($\beta = 0.33, 0.38, \text{ and } 0.25, P < 0.001$, respectively). Chi-squared tests were carried out to evaluate the association between this variable and scores of each used scale, showing a p-value < 0.001 for all tests, which points out that pre-pandemic psychopathology was associated with higher rates of mental health outcomes (data not shown, available upon request).

Chi-squared tests between previous psychiatric or psychological treatment and mental health outcomes:

	Previous psychiatric or psychological treatment (self- reported) n(720)	No Previous psychiatric or psychological treatment (self- reported) n(280)	χ^2	P - value
The Patient Health Questionnaire-9 (PHQ-9)				
< 10	481	140	23.5	$P < 0.001$
≥ 10	239	140		
Mini-Z Burnout Assessment (≥ 3)				
< 3	509	142	34.6	$P < 0.001$
≥ 3	211	138		

The Generalized Anxiety Disorder-7 (GAD-7)				$P < 0.001$
< 10	524	151	31.8	
≥ 10	196	129		
The Impact of Event Scale - Revised (IES-R)				
< 26	427	105	37.6	$P < 0.001$
≥26	293	175		

Q4. Language Quality: GradeB (Minor language polishing)

R. Thank you for this recommendation. We have double-checked potential linguistic problems by fixing typos, agreements, verbal tenses, and inappropriate word use. Thereafter, we send again the manuscript for final checking by our native English editor (Mrs. Julia Mortimer). After all, we believe that the text reads much better and is free of major errors.