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BMJ Open Protective factors against depressive symptoms among Brazilian healthcare workers during the initial stages of the COVID-19 pandemic: a crosssectional study

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ABSTRACT

Objectives This study aims to assess the prevalence of depressive symptoms among healthcare workers and possible factors associated with this outcome (resilience, spirituality, social support, quality of life, among other individual variables). Our hypothesis is that some of these factors can have a protective effect on depressive symptoms.

Design Web-based cross-sectional survey. Setting Participants were recruited online from 16 April to 23 April 2020.

Participants 1043 healthcare workers, predominantly Brazilians, aged 18 years or older.

Primary and secondary outcome measures Depression was the primary outcome, measured using the Patient Health Questionnaire-9 (PHQ-9). Possible protective factors were measured in the following ways: social support was assessed by the modified Medical Outcomes Study Social Support Survey (mMOS-SS); spirituality, religiousness and personal beliefs (SRPB) were evaluated using the 9-item SRPB module of the brief WHO Quality of Life instrument (WHOQoL-SRPB-bref); quality of life was assessed using the brief EUROHIS instrument for Quality of Life (EUROHIS-QoL 8-item); resilience was assessed using the 10-item Connor-Davidson Resilience Scale (CD-RISC 10).

Results 23% met the criteria for depression according to the PHQ-9 scale. Quality of life (B=-3.87 (-4.30 to -3.43), $\beta = -0.37$, p<0.001), social support (B=-0.32(-0.59 to -0.05), $\beta=-0.04$, p=0.022), resilience $(B=-0.19 (-0.23 \text{ to } -0.15), \beta=-0.20, p<0.001), SRPB$ $(B=-0.03 (-0.05 \text{ to } -0.02), \beta=-0.01, p<0.001)$ and physical exercise (B=-0.95 (-1.40 to -0.51), $\beta=-0.08$, p<0.001) demonstrated protective effects against depression.

Conclusion Healthcare workers have a high risk of developing depressive symptoms during the COVID-19 pandemic, especially those working in the front line. However, there are factors that seem to work as protective mechanisms against depression, notably perceived quality of life.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ We evaluated the correlations between depressive symptoms and factors that could be protective against depression, such as resilience, spirituality, social support and quality of life.
- ⇒ Because the questionnaire was shared online via the snowball sampling method, there may be underrepresentation in the study population due to convenience sampling.
- ⇒ We also evaluated individual factors that could be associated with higher levels of depression such as working in the front line.
- ⇒ This is a cross-sectional study, so it does not, necessarily, links cause and effect since both exposure and outcome are evaluated at the same time.

INTRODUCTION

The world has experienced an immense impact since the beginning of the COVID-19 pandemic—declared by the WHO as an international public health emergency-compelling most countries to provide immediate medical support against the rapid spread of the virus. In Brazil, the first confirmed case of COVID-19 was announced on 26 February, 2020. On the last day of 2020, the country had accumulated a total of 7 563 551 confirmed cases and 192 681 deaths due to COVID-19.² In 2021, numbers continued to rise and on 19 June the country had surpassed 500 000 deaths, placing Brazil as the third country with most confirmed cases (behind only the USA and India), and as the second country in number of deaths by the coronavirus disease.²

Over the course of the COVID-19 pandemic, multiple studies have evaluated its consequences on people's psychosocial health, including population-specific effects, particularly on groups that could be at higher risk of distress, such as healthcare workers (HCWs). For instance, a systematic review on the impacts of COVID-19-related fear and anxiety on job attributes associated COVID-19-related fear with higher levels of perceived job insecurity in dentists and decreased job satisfaction, increased psychological distress and intentions of professional turnover among front-line nurses.³ As new cases emerged, HCWs were required to work directly or indirectly with patients with COVID-19 while everyone else was advised to stay home. Physical and mental stress can increase the chances of HCWs developing disorders such as depression, anxiety or post-traumatic stress. 45 Studies have associated the high levels of exposure front-line workers undertake during an epidemic with a higher risk of developing depression or other mental health problems. ⁶⁷ Thus, epidemiological surveys on mental health disorders, trauma-informed care, professional helpseeking and related barriers should be conducted among populations affected by multiple traumatic events during the COVID-19 outbreak. The findings may contribute to coordinate and align response programmes and treatment models beyond national priorities.8

Among the possible impacts that the pandemic could have on mental health, psychiatric disorders such as depression have been frequent concerns. A study which included multiple African countries revealed that depression and anxiety were the most reported psychiatric disorders among HCWs from the beginning of the pandemic in December of 2019 to March of 2021. According to the WHO, depression is one of the main causes of declining health and disability worldwide, leading to suicide in some cases. Its major role in the general global burden of disease means it is classified as a priority condition.¹⁰ A systematic review demonstrated that at least one in five HCWs have reported symptoms of depression and anxiety during the COVID-19 pandemic.¹¹ It is thus important to investigate protective factors against depressive symptoms among HCWs directly or indirectly involved with patients with COVID-19.

Scholars across a range of disciplines have assessed different possible protective and risk factors for depressive episodes and other psychiatric outcomes.⁶ Such factors could be targeted by interventions aiming to mitigate the impact of the COVID-19 pandemic on the mental health of this population. A recent study evaluated possible protective factors on the mental well-being of HCWs and associated clear communication and support from the workplace, as well as social support and personal sense of control with better outcomes.⁶ The aforementioned study conducted in Africa, which affirmed that depression and anxiety were the most frequent psychiatric disorders reported by HCWs, also indicated that low levels of resilience and low social support could increase the risk for these disorders. Protective and risk factors vary according to the population or individual characteristics. Therefore, evaluating different factors is important to assess which factors could have a greater effect on a specific population.¹²

Ouality of life (OoL) is an important element in an individual's life, and it is impacted by different aspects considered as domains or predictors. Although the definition of QoL is not generally agreed in the literature, ¹³ many studies have associated lower perceived QoL with high levels of psychological stress and depression.¹⁴ A recent study presented some important domains or predictors of QoL-including spirituality, religiousness and social support—and demonstrated how they can have a positive impact on mental health and prevent outcomes such as depressive episodes.¹⁵ Conversely, lack of social support and poor perceived social networks have been associated with negative mental health outcomes, 15 16 including severe depressive symptoms and higher suicide rates.¹ Moreover, interventions aiming to expand social networks have shown positive impact on mental health, decreasing risk factors such as loneliness—a common feeling found in people with depression.¹⁸ Furthermore, spirituality, religiousness and personal beliefs (SRPB) have been associated with increased levels of resilience, 19 20 which facilitates dealing with adversities and enables improvements in mental health.²¹

In summary, we aim to (1) assess the prevalence of depressive symptoms among HCWs working directly and indirectly in the COVID-19 pandemic; (2) investigate possible associated factors to this outcome (resilience, SRPB, social support, QoL, among other personal variables) and (3) investigate the impact of the pandemic on front-line workers' depressive symptoms levels. Our hypothesis is that protective factors are associated with better outcomes in relation to depressive symptoms. We also hypothesise that HCWs dealing directly with patients with COVID-19 were more susceptible to develop a depressive episode. Our findings will provide the scientific community and government advisors knowledge about a population that is rarely surveyed in Brazil. Additionally, this study may be helpful to address mental health interventions in HCWs working directly and indirectly with patients with COVID-19.

METHODS Study design

A web-based cross-sectional survey was performed from 16 April to 23 April 2020, when Brazil had 43 079 confirmed cases and 2741 COVID-19-related deaths. The time range was stipulated in an effort to collect and assess the initial stages and impacts of the social isolation suggested by Brazilian and international health authorities to slow the progression of the COVID-19 pandemic. Participants answered a seven-section questionnaire on demographic data and questionnaires containing instruments to assess depression, QoL, social support, SRPB and resilience. It is important to address that HCWs in Brazil include a wide range of professionals: technicians, assistants, therapists, physicians, nurses, among others. Consequently, when referring to these professionals, one must consider the variability of factors such as educational levels and wages.



To increase the range of this survey and make it more accessible for participants, the online protocol was uploaded into a Google Forms survey (Google, Mountain View, California, USA) entitled 'Quality of life in COVID-19 pandemic's social isolation' shared via social media platforms.

Measures

Depression

Primary outcome was evaluated using the Patient Health Questionnaire (PHQ-9). This questionnaire is the depression module of the PHQ, a self-assessment version of the PRIME-MD diagnostic instrument for common mental disorders. PHQ-9 consists of an instrument with diagnostic and severity measurement properties, composed of nine items scored from 0 (not at all) to 3 (nearly every day). The resulting scores indicate the presence and severity of depression as follows: 0–4 (none), 5–9 (mild), 10–14 (moderate), 15–19 (moderately severe) and 20–27 (severe). The PHQ-9 is a widely studied screening tool for depression. It has been validated in Brazil and showed good psychometric properties. In the internal consistency analysis of this study, the PHQ-9 scale had a Cronbach's alpha coefficient of 0.88.

Quality of life

EUROHIS instrument for Quality of Life (EURO-HIS-QOL) 8-item index was created to be a reliable shorter QoL measure based on the WHO Quality of Life instrument (WHOQOL)-100 and its abbreviated form, the WHOQOL-bref, by the WHOQOL group.²⁶ This instrument was initially validated by its creators based on samples of more than 10 European countries, and its psychometric properties have been evaluated in Brazil and compared with its predecessors in studies containing data of multiple countries, being a valid cross-cultural instrument to evaluate QoL. 27 28 It consists of eight items (overall QoL, general health, energy, ability for daily activities, self-esteem, personal relationships, finances and living conditions) and each item score ranges from 0 (eg, very dissatisfied) to 5 (eg, very satisfied), and the result is the sum of all items; higher scores indicate the better perception of QoL. For this measure, Cronbach's alpha was 0.81 in the present study.

Social support

Assessed by the 8-item modified Medical Outcomes Study Social Support Survey (mMOS-SS) which is divided into emotional and instrumental support domains, and each item is scored 1–5, providing an overall functional social support measure, with higher scores indicating higher levels of social support.²⁹ The scale has been validated and showed reliable psychometric properties for multiple population subtypes.^{30–32} In the internal consistency analysis, this scale had a Cronbach's alpha of 0.9.

Spirituality, religiousness and personal beliefs

Measured by the 9-item SRPB module of the WHOQoL-SRPB-bref, an abbreviated scale derived from the

WHOQoL group instrument WHOQoL-SRPB for the assessment of SRPB within QoL.³³ The Brazilian Portuguese version of this instrument has been previously validated and showed adequate psychometric properties, comparable to its extended version and its version in English.³⁴ This instrument consists of eight items that showed the best psychometric properties of the 32-item WHOQoL-SRPB plus one item taken from the psychological domain of the WHOQoL-bref, scored from 1 to 5. In the present study, the SRPB-9 scale had a Cronbach's alpha of 0.87.

Resilience

The 10-item Connor-Davidson Resilience Scale (CD-RISC-10), a short form of the Connor-Davidson Resilience Scale (CD-RISC), both previously validated with reliable psychometric properties. ^{35–37} The 10 items in this instrument are answered in a scale of 0–4, resulting in a score ranging from 0 to 40, in which higher scores indicate higher levels of resilience. ³⁸ For the CD-RISC-10 resilience scale, Cronbach's alpha was 0.88 in this analysis.

Participants

The inclusion of the participants was based on the snow-ball sampling method. The survey was shared via social media platforms, starting from our research group's social network pages (Facebook, Instagram and WhatsApp) and our personal social networks, and then shared outward to reach as many people as possible. All participants declared to be 18 years of age or older and voluntarily agreed to participate by filling out an informed consent form. No incentives were given for participation, but participants were encouraged to share the online survey with their social circles. To ensure confidentiality and anonymity, no direct personal information that could identify participants was requested.

Participants of this research are a part of a bigger sample composed of 3274 people from another study that assessed similar aspects of the general population.³⁹ Data from the participants that identified themselves as HCWs (31.8%) were filtered from the original population to be analysed in this study. Regarding exclusion criteria, respondents who did not declare to be over the age of 18 years or who did not declare to be a HCW were excluded.

Ethics statement

The present study was conducted in accordance with the Declaration of Helsinki, and it was approved by the Research Ethics Committee of the Hospital de Clínicas de Porto Alegre, in Porto Alegre, Southern Brazil and by the Brazilian National Committee of Research Ethics (CAAE 30487620.7.0000.5327).

Patient and public involvement

Patients and or the public were not directly involved in the design, conduct, reporting or dissemination plans for this study.



Statistical analysis

Data were downloaded from Google Forms into Microsoft Excel, and all statistical analyses were performed using IBM's SPSS Statistics V.24.0 (IBM, Armonk, New York, USA). Descriptive statistics (means, SD and frequency) were used to report the general description of the sample. Categorical, non-normally distributed variables from the demographic data questionnaire and their associated PHQ-9 score medians and IQRs were reported, and Mann-Whitney U tests or Kruskal-Wallis tests were used to assess the differences between groups. Spearman correlations were used to evaluate the strength and direction of the relationships between the independent variables (age, resilience, SRPB, social support and QoL) and the PHO-9 scores. Kolmogorov-Smirnov test was used to evaluate the normality and distribution of the data. In addition, probability plots, histograms and scatter plots were created and checked for the linearity, normality and homoscedasticity. The normality tests were taken into consideration in the decision of statistical methods for further analysis. The variables that presented a normal distribution with p values lower than 0.2 and that met the other assumptions analysed in the diagrams and previous correlation analysis were included in a parametric multivariate analysis through linear regression. The internal consistency of the instruments used to evaluate the primary outcome and the possible protective factors were evaluated using Cronbach's alpha. Quarantine length was a dichotomised variable (>30 days or ≤30 days). We computed a multivariate analysis of predictors of depressive symptoms during COVID-19 using linear regressions. To evaluate the subgroups of HCWs who were working directly or indirectly with patients with COVID-19 and the PHQ-9 cut point for depression suspicion, a χ^2 test was conducted between these groups. Statistical significance was considered when p<0.05.

RESULTS

General description

General descriptions of the sample are shown in table 1. In total, 1043 HCWs completed the survey. The mean age was 40.81 years (SD±12.41), and 16.5% were men. The ethnic composition of the sample was 951 (91.5%) whites and 88 (8.5%) non-whites. Most participants were employed (n=863, 83%), had a graduate degree (n=717, 68.9%) or complete higher education (n=191, 18.4%). Approximately half of the participants (n=564, 54.1%) reported being satisfied with their income. Only four (0.4%) participants declared suspecting to be infected with COVID-19. Chronic conditions were reported by 587 participants (68.7%).

About 14.7% of the HCWs (n=153) were working directly with patients with COVID-19, and 62.4% (n=651) of the HCWs were on mental health treatment. From the total of participants, 247 (23.7%) met the criteria for depression according to the PHQ. When performing a cross-tabulation analysis between the variables of directly

Table 1 General description of the sample		
Variable	Health professionals (N=1043)	
Depression*	247 (23.7%)	
Age, mean (±SD)	40.81 (±12.41)	
Gender, n (%)		
Male	172 (16.5)	
Ethnicity, n (%)		
White	951 (91.5)	
Non-white	88 (8.5)	
Marital status, n (%)		
Single	281 (27.1)	
Married or in a couple	661 (63.9)	
Separated or divorced	81 (7.8)	
Widower	12 (1.2)	
Occupation, n (%)		
Retired due to disability	3 (0.3)	
Retired from work	42 (4.0)	
Paid work	863 (83.0)	
Housekeeper	6 (0.6)	
In sickness benefit/sick leave	8 (0.8)	
Student	89 (8.6)	
No condition to answer	12 (1.2)	
Without occupation (not retired)	17 (1.6)	
Education, n (%)		
Incomplete elementary school	1 (0.1)	
Incomplete high school	1 (0.1)	
Complete high school	42 (4.0)	
Incomplete higher education	87 (8.4)	
Complete higher education	191 (18.4)	
Graduate degree	717 (68.9)	
Suspected COVID-19 infection, n (%)	4 (0.4)	
Chronic disease, n (%)	142 (13.6)	
Quarantine length over 30 days	587 (68.7%)	
Mental health treatment	651 (62.4%)	
Attendance of patients with COVID-19	153 (14.7%)	
Income satisfaction	564 (54.1%)	

*According to Patient Health Questionnaire-9 scores. †SD = standard deviation.†

working with patients with COVID-19 or not and the PHQ-9 criteria for depression, the prevalence for depression in those working in the front line was 28.1% with an OR of 1.23 when compared with those who stated to not be working directly with infected patients. However, the χ^2 test failed to reach statistical significance for this association (p=0.161).

Non-parametric tests considering PHQ-9 scores

Bivariate analyses are shown in table 2. Through non-parametric correlations, age (ρ =-0.37), SRPB (ρ =-0.33),



Table 2 Non-parametric analyses considering PHQ-9 scores in healthcare workers

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75)
0.001

^{*}Spearman's rho.

†Evaluated through Mann-Whitney U test or Kruskal-Wallis test. CHE, complete higher education; IEM, incomplete elementary school; IHE, incomplete higher education; PHQ, Patient Health Questionnaire.

social support (ρ =-0.26), resiliency (ρ =-0.47) and QoL (ρ =-0.57) had negative Spearman's rho (ρ) to depressive symptoms and were all statistically significant (ρ <0.001).

Univariate analysis through non-parametric tests demonstrated significant results when evaluating groups medians and IQR by gender, marital status, occupation, education, physical activity and working directly with

Table 3 Multivariate analysis of associated factors of depressive symptoms during COVID-19 guarantine

Predictor	B (95% CI)	Standardised β	P value	
Gender (ref.=female)	-2.0 (-2.51 to -1.42)	-0.12	<0.001	
Age	-0.09 (-0.11 to -0.08)	-0.19	< 0.001	
Quality of life*	-3.87 (-4.30 to -3.43)	-0.37	< 0.001	
Social support†	-0.32 (-0.59 to -0.05)	-0.04	0.022	
Resilience‡	-0.19 (-0.23 to -0.15)	-0.20	< 0.001	
SRPB§	-0.03 (-0.05 to -0.02)	-0.01	< 0.001	
Physical activity	-0.95 (-1.40 to -0.51)	-0.08	<0.001	
Attendance of patients with COVID-19	0.46 (-0.32 to 1.23)	0.02	0.246	
*Evaluated through EUROHIS-QoL-8. †Evaluated through mMOS-SS. ‡Evaluated through CD-RISC. §Evaluated through WHO-QoL SRPB-8. CD-RISC, Connor-Davidson Resilience Scale; EUROHIS-QoL-8, 8- item EUROHIS instrument for Quality of Life; mMOS-SS, modified Medical Outcomes Study Social Support Survey; WHO-QoL-SRPB,				

patients with COVID-19, when analysed with PHQ-9 median (PHQm) and IQR. PHQ-9 scores were higher in participants who were women (PHQm=9, p=0.001), non-whites (PHQm=9, p=0.480), single (PHQm=10.5, p<0.001), unpaid (PHQm=11, p<0.001), from elementary to high school education (PHQm=12, p<0.001), in mental health treatment (PHQm=9, p=0.142), no physical activity (PHQm=10, p<0.001) and in HCWs dealing directly with patients with COVID-19 (PHQm=10, p=0.001).

spirituality, religiousness and personal beliefs module of the WHO

Multivariate analyses of possible protective factors through linear regression

Table 3 shows a multivariate analysis of depressive symptoms predictors during the COVID-19 quarantine through linear regression. Gender (female reference), age, QoL, social support, resilience, SRPB and physical activity had significant differences in PHQ-9 scores. All variables presented a negative standardised β (–0.12 to –0.19, –0.37 to –0.04, –0.20 to –0.01 and –0.08, respectively). Working directly with patients with COVID-19 had a positive standardised β (0.03, 0.07 and 0.03, respectively) but did not present statistical significance (p=0.246).

DISCUSSION

Quality of Life.

The present study found a presence of depressive symptoms in 23% of the HCWs who met the criteria for depression in the PHQ-9 scale during the initial stages of the pandemic. Individual factors such as female gender, lower educational levels, being non-white, single, lack of income, being in mental health treatment and lack of physical activity practice were associated with depressive symptoms.



In the non-parametric correlations using Spearman's rho, QoL, social support, resilience and SRPB showed statistically significant negative coefficients when associated with depressive symptoms, demonstrating protective effects over depression. Being in mental health treatment and suspected COVID-19 infection, while working in the front line were initially associated with higher PHQ-9 scores; however, the results of the analysis failed to reach statistical significance for these associations.

Working in the front line, in direct contact with patients with COVID-19 showed a PHQ-9 median compatible with depression and was statistically significant, evidencing the possible association between working with infected patients and higher levels of depressive symptoms. On the other hand, in the multivariate analysis through linear regressions, working in the front line failed to reach statistical significance.

Multiple studies have evaluated the mental health of HCWs during the COVID-19 pandemic. A meta-analysis and a hospital-based study performed mostly in Wuhan, China, at the beginning of 2020, reported a high prevalence of depression inHCWs of 31.8% and 50.4%, respectively. 40.41 These findings corroborate the hypothesis that these professionals are at a higher risk of developing negative mental health outcomes. On the other hand, few studies evaluated possible protective factors for the HCWs' mental health, in the COVID-19 pandemic. In Spain, a study associating being female with a higher risk of depression, showed that higher levels of resilience had a protective effect against depression. 42 Additionally, studies have also shown social support as a possible protective mechanism. 43.44

The present study, in the multivariate analysis through linear regression for possible predictors of depression, showed that almost all the possible protective factors evaluated had negative coefficients when associated with depressive symptoms, indicating an association with better mental health outcomes. Such evidence suggests that interventions aiming to improve protective factors could be useful in the prevention of depressive episodes in this population. The role that QoL had in reduced levels of depression should be noted, as it was the predictor with the most negative Spearman's rho coefficient and negative β that also reached statistical significance with a CI below zero, showing an inverse relationship between levels of perceived QoL and depressive symptoms.

In more recent studies evaluating the effects of the COVID-19 pandemic on the mental health of HCWs, depression was a frequent finding. However, other mental health conditions have been reported at a concerning rate among these professionals, such as post-traumatic stress disorder, anxiety, psychological distress and insomnia. In a meta-analysis comparing the prevalence of depression symptoms, anxiety, insomnia, post-traumatic stress disorder and psychological distress, HCWs and the general population showed a similarly high prevalence for most of them during the pandemic, except for sleep problems and insomnia which were reported at a higher

rate by HCWs in comparison to the general population during the COVID-19 pandemic, especially among front-line workers. He Interestingly, sleep problems have been associated with depression, anxiety and psychological distress in HCWs during the pandemic and could also be a target for measures aiming to prevent or treat depression and other mental health conditions. He

Strengths and limitations

This study captured some of the possible impacts on the mental health of HCWs during the initial stages of the COVID-19 outbreak in Brazil as data were collected 2 months after the first confirmed case in the country. For this reason, our results may be especially useful for future comparisons with studies conducted at different stages of this pandemic. Furthermore, to the best of our knowledge, no study was conducted in Brazil among health-care professionals working in the COVID-19 pandemic assessing depressive symptoms and possible protective factors during this period.

However, the study limitations should be taken into consideration. First, the research is cross-sectional in design, and as such, it does not, necessarily, link cause and effect since both exposure and outcome are evaluated at the same time. Nevertheless, this limitation introduces the possibility for future surveys to evaluate different time points of the COVID-19 pandemic in this population for a more accurate measure of these associations. Second, the questionnaire was shared online through social networks, and this could lead to convenience or voluntary response bias. On the other hand, this could also explain why-although the study showed a high prevalence of depressive symptoms in HCWs-it was relatively smaller than other studies mentioned before. The sharing of our questionnaire started through our social networks, implying in a large portion of our sample being possibly composed by HCWs primarily in research (therefore, being able to work from home). This is visible in table 1, in which 68.7% of the participants affirmed to be in social isolation for over 30 days. Third, demographic characteristics of participants, for example, the fact that most of our sample hold a graduate degree, and most of it was composed of women could represent a tendency for certain results. Fourth, we did not differentiate the professions (eg, dentists, nurses, psychologists, pharmacists, etc), which could have helped to identify professional groups at a higher risk of depression.

CONCLUSIONS

Our findings demonstrated that HCWs have a higher risk of developing depressive symptoms during the COVID-19 pandemic, especially those working in the front line. However, some associated factors seem to protect against depression, especially perceived QoL, but also social support, resilience, SRPB and physical activity. Therefore, greater attention should be paid to HCWs' mental health. Finally, adapting strategies to reduce depressive



symptoms should be a priority from governmental policies directed to this population.

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Contributors EMJ responsible for the overall content, interpreted the results, conducted the literature review, revised the statistical analyses and wrote the manuscript. LJV helped developing the first drafts and conducting the statistical analyses. AASJ and FCdAC reviewed the article and provided constructive feedback. FCdAC and AMB worked on the questionnaire shared online and collected the data. NSdR is the group's principal investigator, reviewed and approved the final version of manuscript. All authors contributed with the conception and design of the study, reviewed the manuscript and approved the final version of the study.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Research Ethics Committee of the Hospital de Clínicas de Porto Alegre and Brazilian National Committee of Research Ethics (CAAE 30487620.7.0000.5327).

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