

Clinical Research

Has the COVID-19 Pandemic Changed the Daily Practices and Psychological State of Orthopaedic Residents?

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Abstract

Background The coronavirus-19 (COVID-19) pandemic has been an unprecedented time for healthcare and has substantially changed resource availability in surgeons' work practices and routines. Many orthopaedic departments suspended elective surgery, and some re-deployed orthopaedic residents to stressful nonorthopaedic tasks; long hours were

commonplace. Stress-reaction symptoms such as anxiety and depression have been reported in about 10% of healthcare workers during previous infectious-diseases outbreaks (including the Ebola virus), but little is known about the psychological needs of residents faced with this global disaster. **Questions/purposes** (1) Have anxiety and depression symptoms among orthopaedic residents worsened from the period before to the period after the lockdown in Italy? (2) Are there differences in anxiety and depression symptoms between residents who worked in a COVID-19 department and those who did not?

Methods The Italian Association of Orthopaedic and Traumatology Residents is comprised of 365 members who were recruited through the organization's mailing list; they were asked to respond to a survey about their health and well-being at the beginning and end of the first COVID-19 Italian lockdown (March 9, 2020 to May 3, 2020). For the survey's development, 10 orthopaedic surgery residents at the Magna Graecia University of Catanzaro were preliminarily asked to answer the surveys, and both face validity and content validity were tested. The test-retest reliability was 0.9. Impact on and future concerns about family life and daily work practice, as well as sleep disorders, were investigated. Anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS), which includes 14 questions (seven for anxiety, HADS-A; and seven for depression, HADS-D) on a Likert scale (0-3); thus, a patient can have a score between 0 and 21 for either the HADS-A or HADS-D, with higher scores indicating a greater likelihood of anxiety or depression. Previously reported minimum clinically important differences ranged from 1.5 to 1.7. For each scale, total scores of ≤ 7 , 8 to 10, and ≥ 11 were taken to represent normal, borderline, or abnormal level of anxiety or depression,

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respectively. Overall, 75% (272 of 365) of residents completed the survey at both the beginning and end of the lockdown; 72% (196 of 272) were men, the mean \pm SD age was 30 ± 3 years, 72% (197 of 272) worked in a hospital setting with patients who were COVID-19-positive, 20% (55 of 272) served in a COVID-19 department, and 5% (7 of 139) tested positive for COVID-19 by nasal-pharyngeal swab. Overall, 9% (24 of 272) of residents had family members who contracted COVID-19, and 3% (8 of 272) had a relative who died. Because of the risk of possible COVID-19 exposure, 18% (48 of 272) of residents needed to temporarily change their household given that social distancing was considered the best way to slow the spread of COVID-19.

Results At the end of the lockdown, orthopaedic residents exhibited signs of worsening anxiety and depression as measured by the overall HADS score (median 9 [IQR 5 to 14] versus median 11 [IQR 6 to 17.8], respectively; median difference -1 [95% CI -1.5 to -0.5]; effect size [r] = -0.24; $p < 0.001$) as well as in the depression subscale (median 4 [IQR 2 to 7] versus median 5.5 [IQR 3 to 8], respectively; median difference -1 [95% CI -1.5 to -0.5]; $r = -0.36$; $p < 0.001$). We found no difference in the development of anxiety or depression between residents who worked in a COVID-19 department and those who did not, as demonstrated by comparing the change in HADS scores between these groups (median 1 [IQR -3 to 4] versus median 1 [IQR -2 to 4] in HADS change score over time; median difference 0 [95% CI -1 to 2]; $r = -0.03$; $p = 0.61$).

Conclusion The COVID-19 pandemic has affected the daily practice of orthopaedic residents and has had important, far-reaching consequences on their health and well-being, including social implications. Residents showed higher anxiety and depression symptoms at the end of the lockdown. No differences were found in changes of anxiety and depression, over time, for residents who worked in a COVID-19 department compared with those who did not. The evaluation of anxiety and depression through standardized questionnaires could help to identify residents at risk of higher psychological distress who could be referred to regular psychological counseling as a possible prevention strategy during stressful times. Future studies should confirm the long-term effects of these findings.

Level of Evidence Level II, prognostic study.

Introduction

Italy was one of the first European countries to be affected by coronavirus-2019 (COVID-19). The rapid and wide spread of COVID-19 in Italy led the government to implement strict quarantine measures, initially sealing off the northern regions followed by the entire country. From March 9, 2020 to May 3, 2020, to mitigate spread of the virus, citizens could move only within the boundaries of their municipality of residence. Several hospitals were converted into partial or full COVID-19

centers, and health personnel adapted to cope with this new disease to treat a large number of patients with the disease. Although orthopaedic and traumatology residents were not the first-choice physicians for these new COVID-19 departments, in some Italian regions, they were required to contribute clinical efforts in these new settings. COVID-19 substantially changed the resource availability of the healthcare system and surgeons' work practices and routines [3, 11, 23]; most orthopaedic units stopped performing elective procedures in their departments, and they were only allowed to perform emergency treatments.

Stress-reaction symptoms such as anxiety and depression have been reported in about 10% of healthcare workers during previous infectious-diseases outbreaks (including that of the Ebola virus) [20], but little is known about the psychological needs of orthopaedic residents who delivered care during the COVID-19 pandemic. We therefore developed a multicenter survey to evaluate the daily practices of orthopaedic and trauma surgery residents and the psychological impact of the COVID-19 pandemic on them during the Italian lockdown. The results may assist residency programs and healthcare professionals in safeguarding the psychological well-being of orthopaedic residents during the COVID-19 pandemic and others that may arise in the future.

We therefore asked: (1) Have anxiety and depression symptoms among orthopaedic residents worsened from the period before to the period after the lockdown in Italy? (2) Are there differences in anxiety and depression symptoms between residents who worked in a COVID-19 department and those who did not?

Materials and Methods

Study Design and Setting

The Associazione Italiana Specializzandi in Ortopedia e Traumatologia (Italian Association of Orthopaedic and Traumatology Residents) is comprised of 365 members who were asked to complete a survey on their health and well-being at the beginning and end of the first COVID-19 national lockdown (March 9, 2020 to May 3, 2020). An online questionnaire was built using Google Forms (Google LLC), a free, open-source software survey tool. Residents were recruited through a mailing list associated with the Italian Association of Orthopaedic and Traumatology Residents, and they received a detailed description of the study along with an email invitation to participate in the survey. Data acquisition was prospective.

Survey Instruments

For the survey's development, 10 orthopaedic surgery residents at the Magna Graecia University of Catanzaro were

preliminarily asked to answer the surveys, and the face and content validity were tested. The survey fully covers the area of interest; the Hospital Anxiety and Depression Scale (HADS) has been demonstrated to be a reliable and valid measure for assessing mental health in the Italian population [5], and it has been applied in studies related to the COVID-19 pandemic [24]. The survey took approximately 10 to 15 minutes to complete, and it was administered twice, with a 7-day interval. The test-retest reliability was 0.9, which was considered excellent. All respondents provided informed consent at the beginning of the survey with a yes-no question confirming their willingness to participate. Nonrespondents were sent an email reminder.

Anxiety and depression were assessed at the beginning and end of lockdown using the HADS [28]. This valid and reliable tool [5] refers to what an individual has experienced over the past week, and it includes 14 questions (seven for anxiety, HADS-A; and seven for depression, HADS-D) on a Likert scale (0-3); thus, a patient can have a score between 0 and 21 for either the HADS-A or HADS-D, with higher scores indicating a greater likelihood of anxiety or depression. The previously reported minimum clinically important differences (MCIDs) were 1.5 [22] and 1.7 [14] in two studies on the topic. For each scale, final scores of ≤ 7, 8 to 10, and ≥ 11 were considered to represent normal, borderline, or abnormal levels of anxiety or depression, respectively.

Participants

The participants were identified anonymously using an identification code that each of them needed to enter before completing the survey at the beginning of the lockdown. The same code was required before completing the survey at the end of the lockdown. Three hundred sixty-five Italian orthopaedic and trauma surgery residents were asked by email to complete surveys. Two participants completed the survey only at the beginning of lockdown but did not respond to the second survey after lockdown, so their results were excluded. Ninety-one residents did not participate in the survey. Thus, we analyzed data on 75% (272 of 365) of our participants, all of those who completed both surveys.

Residents were asked to define their hospital working setting. A COVID-19 department was defined as an emergency department that treated patients with COVID-19 from screening to treatment. Thus, residents were considered globally or divided into two groups: those who worked, at least partially, in a COVID-19 department and those who did not.

The residents had a mean age of 30 ± 3 years, and 72% (196 of 272) were men. They were approximately evenly distributed throughout Italy and among residency years (Table 1). Seventy-two percent (197 of 272) worked in a

hospital setting with patients who were COVID-19-positive, and 20% (55 of 272) of residents served in a COVID-19 department, at least partially, and cared for patients with a positive test result for COVID-19.

At the end of the lockdown, residents were asked whether they had nasal-pharyngeal swabs for COVID-19 research or if family members became infected or died during the survey period. Fifty-one percent (139 of 272) of the residents underwent at least one nasopharyngeal swab test, and 5% (7 of 139) had positive test results. Considering relatives, 9% (24 of 272) of residents had family members who contracted COVID-19. Eight participants' family members died among the 24 family members who tested positive for COVID-19. Overall, 3% (8 of 272) of residents had a relative who died. At the end of lockdown, residents were in various home conditions: 32% (86 of 272) lived alone, 39% (105 of 272) had two people at home, 14% (39 of 272) had three, 11% (31 of 272) had four, and 4% (11 of 272) had five or more people at home. During the survey period, because of the risk of possible COVID-19 exposure, 18% (48 of 272) of residents needed to change their homes temporarily given that social distancing was considered the best means to slow the spread of COVID-19.

Baseline Between-group Differences and How They Were Handled

There were no differences in baseline HADS score and anxiety and depression subscales between residents

Table 1. Baseline characteristics of Italian orthopaedic residents in this study (n = 272)

Characteristic	Mean ± SD or % (n)
Women	28 (76)
Age in years	30 ± 3
Working area	
North	38 (103)
Center	35 (94)
South	28 (75)
Residency year	
1	28 (75)
2	17 (46)
3	23 (62)
4	17 (47)
5	15 (42)
Ongoing surgical subspecialty	
Traumatology	53 (143)
Orthopaedics	40 (108)
Oncology	4 (12)
Pediatrics	3 (9)

who worked in a COVID-19 department and those who did not. In detail, in those groups, no differences were found in the overall HADS score (median 10 [IQR 6 to 15] versus median 9 [IQR 5 to 13.5]; median difference -2 [95% CI -3 to 0]; $p = 0.103$), in HADS-A (median 5 [IQR 2 to 9] versus median 5 [IQR 3 to 8]; median difference -1 [95% CI -2 to 0]; $p = 0.136$) and HADS-D (median 5 [IQR 4 to 8] versus median 4 [IQR 2 to 6]; median difference -1 [95% CI 0 to 2]; $p = 0.149$). To avoid possible bias, we compared changes in overall HADS score, HADS-A, and HADS-D subscales over time.

Ethical Approval

Ethical approval for this study was waived by our institution owing to the noninvasive methods of data acquisition.

Statistical Analysis

Data are reported as the percentages and absolute numbers, as the means and SDs, or as the median and interquartile range (IQR), whenever applicable. We assessed the data distribution with the Kolmogorov-Smirnov normality test. Based on this preliminary analysis, we adopted non-parametric tests (Wilcoxon signed-rank and Mann-Whitney U tests). We used a chi-square test to identify differences in the proportion of residents whose HADS-A and HADS-D scores were categorized as normal, borderline, or abnormal before and after lockdown. Further comparisons were performed between residents involved in the care of patients with COVID-19 and those not involved in their care and between men and women. The results were collected and analyzed using Excel (Microsoft) and IBM SPSS version 21.0.0.1 (IBM Corp). Statistical significance was set at a p value < 0.05 ; according to the Bonferroni correction, the statistical significance for the chi-square test was set at a p value < 0.025 when 3×2 contingency tables with two degrees of freedom were reported.

Results

Change in Anxiety and Depression Symptoms Before and After Lockdown

From before to after the lockdown, orthopaedic residents exhibited signs of worsening anxiety and depression as measured by the overall HADS score (median 9 [IQR 5 to 14] versus median 11 [IQR 6 to 17.8], respectively; median difference -1 [95% CI -1.5 to -0.5]; effect size $[r] = -0.24$; $p < 0.001$) as well as in the depression subscale of that score (median 4 [IQR 2 to 7] versus median 5.5 [IQR 3 to 8], respectively; median difference -1 [95% CI -1.5 to -0.5]; $r = -0.36$; $p < 0.001$)

There were no differences in the HADS-A score (median 5 [IQR 3 to 8] versus median 5 [IQR 3 to 9], respectively; median difference 0 [95% CI -0.5 to 0]; $r = -0.06$; $p = 0.30$). These data were confirmed in a further analysis comparing differences in the proportion of residents whose anxiety and depression subscale scores were categorized as normal, borderline, or abnormal before and after lockdown (Table 2).

We found no difference in HADS scores between before and after the lockdown for residents who worked in a COVID-19 department (median 10 [IQR 6 to 15] versus median 12 [IQR 7 to 17], respectively; median difference -1 [95% CI -2.5 to 0.5]; $r = -0.17$; $p = 0.22$).

Residents who worked in a non-COVID-19 department had increased HADS scores after the lockdown (median 9 [IQR 5 to 13.5] versus median 10 [IQR 6 to 18], respectively; median difference -1 [95% CI -2 to -0.5]; $r = -0.26$; $p < 0.001$). Furthermore, residents who worked in a non-COVID-19 department reported a worsening of depression subscale scores between the beginning and end of the lockdown (median 4 [IQR 2 to 6] versus median 5 [IQR 2 to 9], respectively; median difference -1 [95% CI -1.5 to -0.5]; $r = -0.40$; $p < 0.001$) (Table 3). These findings were confirmed in a further analysis comparing differences in the proportion of residents whose HADS-A and HADS-D scores were categorized as normal, borderline, or abnormal before and after the lockdown (Table 4).

Concern and worries among residents about further changes that could upset their work were also recorded, and

Table 2. Changes in the categorized HADS subscale values over time among orthopaedic residents ($n = 272$)

	Anxiety scale			Depression scale		
	At the beginning of lockdown	At the end of lockdown	p value	At the beginning of lockdown	At the end of lockdown	p value
Normal	71 (194)	66 (179)	0.30	79 (215)	68 (184)	0.006
Borderline	19 (53)	21 (58)		14 (39)	19 (52)	
Abnormal	9 (25)	13 (35)		7 (18)	13 (36)	

Data presented as % (n); statistically significant p values presented in bold.

Table 3. Median changes in HADS subscale values over time between the group of orthopaedic residents working in a COVID-19 department and those who did not

COVID-19 department residents	Beginning of lockdown (n = 55)	End of lockdown (n = 55)	Difference of medians (95% CI)	p value
HADS Anxiety Scale	5 (2 to 9)	6 (3 to 8)	0 (-1 to 0.5) Effect size = -0.04	0.76
HADS Depression Scale	5 (4 to 8)	6 (4 to 9)	-0.5 (-1.5 to 0) Effect size = -0.23	0.09
Non-COVID-19 department residents	Beginning of lockdown (n = 217)	End of lockdown (n = 217)	Difference of medians (95% CI)	p value
HADS Anxiety Scale	5 (3 to 8)	5 (3 to 9)	0 (-0.5 to 0) Effect size = -0.07	0.32
HADS Depression Scale	4 (2 to 6)	5 (2 to 9)	-1 (-1.5 to -0.5) Effect size = -0.40	< 0.001

Data are presented as median (interquartile range); statistically significant p values presented in bold.

64% (173 of 272) of residents showed fear regarding the future of their career, especially in their surgical training program and a decrease in job and economic opportunities. Based on these factors, 32% (86 of 272) of residents considered modifying their personal goals, such as when or whether to have children. Sleep disorders were reported in 33% (91 of 272) of residents; insomnia and nightmares were the most common (in 71% [65 of 91] and 26% [24 of 91] of residents, respectively).

Residents were asked whether their confidence in returning to a social-health situation was equal to or better than that before the COVID-19 pandemic. Overall, 54% (146 of 272) of residents reported being uncertain on this point, and 3% (8 of 272) reported that they felt certain that they would not return to a social

situation as good or better than before; only 6% (15 of 272) reported full certainty.

Anxiety and Depression: Those Who Worked in COVID-19 Departments versus Those Who Did Not

We found no difference in the development of anxiety or depression between residents who worked in a COVID-19 department and those who did not, as demonstrated by comparing the changes in HADS scores between these groups (median 1 [IQR -3 to 4] versus median 1 [IQR -2 to 4] in HADS change score over time; median difference 0 [95% CI -1 to 2]; r = -0.03; p = 0.61). We found no differences in the anxiety subscale by comparing the change in HADS-A scores

Table 4. Changes in categorized HADS subscale values over time between the group of orthopaedic residents working in a COVID-19 department and those who did not

COVID-19 department residents	Anxiety scale			Depression scale		
	At the beginning of lockdown (n = 55)	At the end of lockdown (n = 55)	p value	At the beginning of lockdown (n = 55)	At the end of lockdown (n = 55)	p value
Normal	69 (38)	64 (35)	0.85	71 (39)	67 (37)	0.83
Borderline	18 (10)	22 (12)		16 (9)	22 (12)	
Abnormal	13 (7)	15 (8)		13 (7)	11 (6)	
Non-COVID-19 department residents	At the beginning of lockdown (n = 217)	At the end of lockdown (n = 217)	p value	At the beginning of lockdown (n = 217)	At the end of lockdown (n = 217)	p value
Normal	72 (156)	66 (144)	0.31	81 (176)	68 (147)	0.001
Borderline	20 (43)	21 (46)		14 (30)	18 (40)	
Abnormal	8 (18)	12 (27)		5 (11)	14 (30)	

Data presented as % (n); statistically significant p values presented in bold.

between residents who worked in a COVID-19 department and those who did not (median 0 [IQR -2 to 2] versus median 0 [IQR -1 to 2] in HADS-A change score over time; median difference 0 [95% CI -1 to 1]; $r = -0.01$; $p = 0.81$). Similarly, we found no differences in the depression subscale by comparing changes in HADS-D scores between residents who worked in a COVID-19 department and those who did not (median 1 [IQR -1 to 4] versus median 1 [IQR 1 to 4] in HADS-D change score over time; median difference 0 [95% CI 0 to 1]; $r = -0.05$; $p = 0.40$).

Discussion

To expand bed capacity for patients who have COVID-19, many inpatient units have been converted to wards that treat patients with COVID-19. Worldwide, elective surgery is being deferred, outpatient visits are being reduced, and orthopaedic residents and fellows are being asked to make drastic changes to their daily routines. The current study examined the psychological impact of COVID-19 on 272 Italian orthopaedic residents, many of whom cared for patients with COVID-19, and approximately 1 in 20 of whom tested positive themselves. We found that the pandemic had an important social impact on orthopaedic residents' perceptions and emotional well-being: 33% (91 of 272) of residents reported sleep disorders and considered modifying their personal lives, and 64% (173 of 272) of residents were fearful about their future surgical education during residency. We also found that the pandemic had consequences on residents' mental health, including a clinically important worsening in HADS scores after the national lockdown and in the depression subscale of that score.

Limitations

This study has several limitations. First, given the study's cross-sectional design, it was difficult to draw firm conclusions regarding the long-term effect of the current pandemic. Second, selection (nonresponse) bias cannot be excluded because 25% of contacted residents did not respond to the survey. However, as reported elsewhere [12], a response rate of 60% has been used as the threshold of acceptability by some. We believe our respondents were representative of Italian residents because they were evenly distributed among the regions of the country and among residency years, although we could not analyze nonrespondents' other characteristics in any specific way. Because of the fluid nature of the COVID-19 pandemic, our findings may not be relevant to all countries. Moreover, this pandemic led to differences in the number and severity of COVID-19 cases throughout Italy. However, with a sample representing almost all regions of the country, the study data are likely generalizable to Italy, where infection and mortality

rates were similar to those of other European countries, and so we believe our findings generalize outside the borders of Italy, as well, to other countries that were affected similarly to our own. Lastly, although we used a validated tool [5] to evaluate anxiety and depression, we did not evaluate other psychological disorders or stress scales. We note, however, that the test-retest reliability on our study's survey instrument was excellent. We also could not query for some additional factors such as history of chronic medical conditions, psychiatric disorders, and major life events that may be associated with anxiety and depression.

Change in Anxiety and Depression Symptoms Before and After Lockdown

We found that after the lockdown, orthopaedic residents demonstrated a clinically important worsening in depression. One article suggested that the COVID-19 pandemic might substantially affect the mental health of healthcare workers [8], and a systematic review [20] reported a high prevalence of depression, anxiety, and insomnia among healthcare professionals. We are not surprised that there have been differences in depression but not in anxiety, as our results are in line several studies with somewhat similar findings. One such study [27] investigated anxiety and depression in the first-line medical staff fighting against COVID-19 in Gansu province, China, and reported that the prevalence of anxiety and depression symptoms was 11% and 46%, respectively. Moreover, a cross-sectional survey [6] conducted in Turkey expressed concerns about the psychological well-being of physicians during the pandemic and showed that 65% had depressive symptoms and 52% had anxiety. A meta-analysis suggested that the proportion of depression in the general population has been seven times higher during the COVID-19 pandemic [2]. Past epidemics, such as SARS and Ebola, were contained more quickly and, despite a higher mortality rate, infection rates were lower, which may explain the prevalence of lower rates of depressive symptoms in those epidemics [10]. However, we do note that a high correlation between the anxiety and depression subscales has been observed in two studies [1, 4]. Watson et al. [25] stated that despite the apparent distinctiveness of anxiety and depression, it can sometimes be difficult to distinguish these conditions.

We reported that among residents tested for COVID-19 by nasal-pharyngeal swab, 5% (7 of 139) of them had a positive result. A survey conducted among members of the Federation of Orthopaedic and Trauma Trainees in Europe reported that 2.2% of 327 participants had a positive test result for COVID-19 [19]. We also found that 9% (24 of 272) of participants' family members contracted COVID-19, and 3% (8 of 272) of residents had a relative who died. Mazza et al. [18] reported that having an acquaintance who

was infected with COVID-19 was associated with increased depression and stress, whereas having an infected relative was associated with increased anxiety in the general population. Based on these findings, we believe residency programs could refer residents to regular psychological counseling as a possible prevention strategy to minimize the impact on mental health during stressful times.

Finally, we found that 33% (91 of 272) of residents experienced sleep disorders, 71% (65 of 91) of whom reported insomnia. Pappa et al. [20] found that the prevalence of insomnia among healthcare workers during the COVID-19 pandemic was 39%. Other authors [9] reported that the prevalence of poor sleep quality in the Chinese public was 18%, and healthcare workers reported the highest proportion (24%) compared with people in other occupational groups. Working time and labor intensity of healthcare workers increase during severe epidemics [16], and these workers often do not have enough time to rest. Healthcare workers are also prone to chronic psychological distress, which is highly correlated with poor sleep quality [13]. Reduced opportunities for physical activity are an additional long-term health-damaging burden [21].

Anxiety and Depression: Those Who Worked in COVID-19 Departments versus Those Who Did Not

We found no difference in the change of HADS scores, over time, for residents who worked in a COVID-19 department in comparison with those who did not. This result was further confirmed by the changes in anxiety and depression subscales in those groups over time. These findings were unexpected because residents in COVID-19 departments were believed to be exposed to more negative experiences. Indeed, our findings contrast with those reported by Lu et al. [15], who found that medical staff working in departments in close contact with patients who have COVID-19, such as the respiratory department, emergency department, intensive care unit, and infectious diseases department, had more psychological disorders and had higher scores for fear, anxiety, and depression than did low-risk contact medical staff and nonclinical staff. However, it should be considered that this study was undertaken in China, which was the first country to face the COVID-19 pandemic. China was unable to predict the evolution of COVID-19 and anticipate a response as opposed to countries that were struck weeks or months later [17]. Reliable leadership and staff training for the task and associated challenges are important factors in the reduction of mental health problems in frontline residents [7, 26]. In this light, the less prepared are more vulnerable, and that must be considered when delineating mental health interventions in the future, as suggested by Machado et al. [17].

Conclusion

The COVID-19 pandemic has affected the daily practice of orthopaedic residents and has had important, far-reaching consequences for their health and well-being, including social implications. In this study, residents showed higher anxiety and depression symptoms at the end of the first national lockdown. No differences were found in changes of anxiety and depression over time for residents who worked in a COVID-19 department compared with those who did not. The evaluation of anxiety and depression through standardized questionnaires could help to identify residents at risk of higher psychological distress who could be referred to regular psychological counseling as a possible prevention strategy to minimize the impact on mental health during stressful times. Future studies should confirm the long-term effects of these findings.

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