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Longitudinal Assessment of Mental Health Consequences of the COVID-19 Pandemic Long-Term Exposure on Health Care Workers from a North West Italian Hospital

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Original Research

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Abstract

Objective: To assess individual variation in anxiety, stress disorder, depression, insomnia, burnout, and resilience in health care workers (HCWs), 12 and 18 months after the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic.

Methods: Prospective longitudinal study.

Results: A total of 207 HCWs (74% female, 46% physicians, 44% nurses) answered; 50% scored over the cut-off for anxiety (GAD-7), 66% for PCL-C, 41% for depression (PHQ-9), 25% for ISI, and 15% started sleep inducers; 52% showed emotional exhaustion (EE), 68% detachment (DE), 39% professional efficacy (EF) at MBI; 27% completed the follow-up questionnaire 6 months later, showing a significant reduction in nearly all scores (GAD-7 median 11[5-15] vs 7[4-12] ($P < 0.001$); PCL-C 43[30-58] vs 37[24-50] ($P < 0.05$); PHQ-9 10[4-16] vs 6[3-12] ($P < 0.001$); ISI 10[4-15] vs 7[5-12](*NS*); MBI EE 25[16-35] vs 23 [15-31] (*NS*), DE 13[8-17] vs 12[8-17], EF 29[25-34] vs 30[25-34]. Living in a flat (OR 2.27 [1.10-4.81], high-intensity-of-care working (2.83 [1.15-7.16] increased risk of anxiety (GAD-7); age between 31-40 y (OR 2.8 [1.11-7.68], being a nurse (OR 3.56 [1.59-8.36] and high-intensity-of-care working (OR 8.43 [2.92-26.8] increased risk of pathological stress (PCL-C).

Conclusions: Nearly half of HCWs showed psychological distress, especially nurses, women, and the youngest. A mandatory job change, increasing intensity of care, working in a COVID-19 department, and being infected were negative factors; having a partner and living in a detached house were protective. Six months later, all the psychological domains showed individual improvement.

It is well known that health care workers (HWCs) who were directly involved in disasters, humanitarian emergencies, Ebola outbreaks, and pandemic emergencies showed significantly higher depressive, anxious, and posttraumatic stress disorder (PTSD) symptoms.[1] In the last 2 years, thousands of HCWs around the world have been exposed to multiple additional stressors in responding to the coronavirus disease (COVID-19) pandemic.[2–4] In the first phase, the lack of information, the shortage of personal protective equipment (PPE), the risk of contracting the infection and of potentially transmitting the virus to loved ones, the sudden overload of working demand, the need of reorganization of the hospital system, the emotional exposure to patients that suffer and die in isolation, the perceived lack of control, and unprecedented ethical concerns were reported as major stressors.[5,6] In the second phase, once the previous issues had been resolved, the workforce had increased and reorganization was achieved, new safety procedures had been assimilated and the therapeutic protocols had been consolidated, the psychosocial problems related to the ongoing epidemic became evident, and public opinion toward HCWs changed.[5,6] The burden of bureaucracy, the long-lasting of the excessive and prolonged stressors, and the restriction of activities that could improve psychological resilience were described as ongoing determinants of fatigue and burnout.[5–7]

In the first months of 2021, the availability of vaccines made it possible to vaccinate all HCWs, who consequently perceived the chance of controlling the pandemic and probably felt able to resume social activities. The relaxation of restrictions, in the following months, could also have contributed to improvement in anxiety and depressive symptoms,[8,9] while the effect of burnout, dissatisfaction, and the intention to quit their job[9] started to appear after 6 months from a traumatic event.[10,11]

In the very extensive mental health literature that described the negative stressors and negative symptoms after the first COVID-19 wave,[12–16] many studies are cross-sectional or retrospective,[6,9,15–17] lacking a pre-post effect[15–18] or a control group.[15–20] Moreover, the

majority of the studies describe a monocentric cohort, limited both geographically and for the professional roles (eg, limited to intensivists[15,16] and to nurses).[15,16,18–20] Many studies used questionnaires,[9–16,19,20] many evaluated burnout alone,[17,18] a few evaluated with validated tools depression, anxiety, and insomnia,[9,15–17] thus limiting the comprehensive assessment of complexity and the systematic description of the psychological response. Regional differences were observed, mainly related to a different burden of COVID-19 cases[3,4,18–21] or cultural differences[11,14,21,22] or organizational issues.[9,10,15–20] A worse psychological burden was observed in younger HCWs, in females and the nurse category, irrespective of ethnic and cultural differences[9–20]; nevertheless, the role of other possible personal and organizational modifiers is still controversial.[9–20]

The biggest studies published so far have been conducted online and anonymously, merely comparing prevalence and mean values, without the possibility of tracking respondents and assessing changes in individual stress exposure and appearance of mental disorders.[1–6,11–13] Moreover, only a few studies evaluated HCWs' distress after the first year of the pandemic and beyond.[6,9,10,15,22,23]

This prospective longitudinal study aimed to evaluate with validated tools the prevalence of anxiety, depression, stress, burnout, and resilience in HCWs of a University Hospital in the Piedmont region, 1 year after the beginning of the pandemic and 6 months later. Secondarily, we evaluated the role of personal and environmental coping factors and potential additional stressors on the psychological outcomes.

Methods

This prospective longitudinal study follows STROBE guidelines for reporting observational studies.[24]

Population

All the workers in the AOU San Luigi Gonzaga were emailed and invited to participate in our survey (nurses, doctors, health care assistants, radiology technicians, administrative and security workers). Their answers were collected anonymously on the SurveyMonkey online platform. Participation was completely voluntary and not economically incentivized. Participants were enrolled in March 2021, and a second assessment took place in August 2021. Individual answers at baseline and after 6 months were matched by a unique code. A reminder mail was sent 15 days after the first and second assessments.

Mental Health Assessment Tools

To assess anxiety, depression, PTSD, insomnia, burnout, and resilience, we used internationally validated scales previously used by other authors[9,10,15,16,20,22] and already validated in the Italian translation.

The 2006 GAD-7 by Spitzer et al.[25] was used for anxiety evaluation. It consists of 7 questions which are answered through a 4-item Likert scale (not at all, several days, more than half the days, nearly every day). Values above 8 are associated with pathological anxiety levels. GAD-7 is a self-administered patient questionnaire used as a screening tool and severity measure for generalized anxiety disorder (GAD), with a sensitivity of 89% and a specificity of 82%. It is moderately good at screening 2 other common anxiety disorders: panic disorder (sensitivity 74%, specificity 81%) and social anxiety disorder (sensitivity 72%, specificity 80%).[26]

PCL-C was chosen to assess posttraumatic stress. It is the civilian version of PCL-M by Weathers et al. from 1994, a reduced form of PCL-5.[27] Through 17 questions, which are answered with a 5-point Likert scale, a high probability of the presence of PTSD is outlined in those who reach scores over 29. The measure provides a total score as well as symptom cluster scores for items related to intrusions, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity. The PCL-C has demonstrated strong psychometric properties, with good-to-excellent internal consistency across subscales, good test–retest reliability, convergent validity, and sensitivity to detect clinically significant levels of PTSD symptoms.[28]

Patient Health Questionnaire-9 (PHQ-9) was chosen to study depressive symptoms. PHQ-9 was found to be an effective method for screening the prevalence and severity of depression. Scores over 10, after having answered the 9 questions using a 4-point Likert scale, identify a moderate-to-severe depressive condition. A 10th question frames the global functional impairment.[29] PHQ-9 scores > 10 had a sensitivity of 88% and a specificity of 88% for major depressive disorder.

The ISI score, Insomnia Severity Index, was used to assess the perceived quality of sleep. It consists of 7 questions that outline the degree of insomnia and how much this affects the subject's quality of life. Values over 14 configure insomnia of at least moderate entity.[30] A cutoff score of 14 (suggesting moderate to severe insomnia) was associated with specificity indices of 98.3% and 100% in the community and clinical samples, respectively, and with sensitivity indices of 47.7% and 78.1% for the 2 samples.[30]

The Maslach Burnout Inventory (MBI), as the Italian translation of the MBI-HSS (human service survey), was used to quantify the degree of burnout.[31–34] This score investigates 3 areas through 22 items that are answered through a 6-point Likert scale: emotional exhaustion (EX), cynicism or detachment from work (DE), and fulfillment or professional efficacy (EF). A score is obtained for each subsection.

The cutoffs are above 8 for DE, above 23 for EX, and below 30 for inadequate personal and professional EF. Burnout is diagnosed when high EX, high DP, and low professional EF are present.[31,32,34] MBI-HSS showed a 92.2% sensitivity and 92.1% specificity in screening the existence of burnout.

CD-RISC, the Connor Davidson Resilience Scale,[35] was used to assess individual resilience. This score evaluates the coping skills of stress: higher scores correspond to greater resilience skills.

Personal Modifiers, Exposure to Stressors, and Resilience Cofactors

We collected demographic data, work role and seniority, level of education, marital status, and usual baseline physical and psychological condition, recording also previous psychiatric diagnosis. We investigated the presence of stressful elements: increased workload, increased emotional burden, mandatory ward change or transfer to ICU, working in COVID-19 units, equipment's shortage, social stigma, and contagion risk. We assessed the composition of the family unit, housing situation, cohabitation with minors or frail people, family support needs, and the presence of other non-work stressors during the lockdown period that may have influenced the psychological state.

Participants were also asked to describe whether they had nutrition disorders or alcohol and drugs abuse during the study period, whether they received a new psychiatric diagnosis, and whether they needed psychological support. We also asked whether they

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were affected by COVID-19 or exposed to infection of relatives or colleagues.

The respondents gave their informed consent to complete the questionnaire, whose answers were collected anonymously by creating a personalized identification code to associate the first phase answers with those of the second one.

The study was approved by the Ethics Committee of our hospital (num 45/2021; Registro di Protocollo Generale AOU San Luigi Gonzaga n°2876 del 22/02/2021).

Statistics

In consideration of the prevailing non-normal distribution of the variables under examination, the continuous variables have been described with median and interquartile range, categorical variables as absolute frequencies and percentage of the total. We compared the results of the questionnaires collected in March and after 6 months for each patient, using the Wilcoxon test for paired data. Individuals were grouped by sex, age group, and job role. Univariate comparisons between the different groups of individuals through tests of Wilcoxon (for comparison between 2 groups) and Kruskal-Wallis (for comparison between more than 2 groups) were performed. Furthermore, the variables of exposure to contagion, personal, family, and home situation were considered as possible modifiers of the response. The chi-square test was used to compare categorical variables across multiple groups when applicable. Psychological distress was expressed both as the result of the score and as having symptoms under and over pathologic thresholds as defined above. Finally, a multivariate analysis was carried out using logistic regression to evaluate the weight of the diverse factors, which showed differences in the univariate analysis, on psychological outcomes. These results were expressed as an odds ratio (OR) with the relative confidence interval of 95%.

The P values were considered significant if < 0.05. All analyses were bidirectional. The R version 4.0 software was used.[36]

Results

We obtained 207 complete answers from the first questionnaire. Participants were equally distributed by age (21% under 30 years (y) of age, 25% 30-40 y, 26% 40-50 y, 24% 50-60 y), mostly female (74.4%) workers. Of those taking part, 45.7% were physicians and 43.7% were nurses. Demographic characteristics, working roles and seniority, personal condition, and living situation are described in Table 1. Only 7.5% of participants had a history of psychiatric disease or were on psychiatric treatment.

Most participants (65.6%) had been working in COVID-19 wards and 36.4% changed their usual work (9.7% voluntarily and 26.7% forcedly); 61.8% worked in an increased level of care environment; 32.8% had contracted COVID-19. Most of the workers (21%) who had contracted the infection had mild symptoms that did not require treatment or were completely asymptomatic (3.6%); 27% had to cohabit with a relative affected by COVID-19; 38.2% had a relative affected and 7.8% a relative with critical illness; 96.9% had affected colleagues; 44% had symptoms; and 7% had symptoms with critical illness (see Table 1).

The median value of GAD-7 scale was 9 (5–14), identifying the presence of clinically relevant anxiety disorder in 50% of the respondents. The median PCL C score was 42 (27–54) with a stress disorder of at least moderate severity in 66% of cases.

The median PHQ-9 was 9 (4–14) in our population, with only 41% of the participants with a clinically relevant depressive disorder. CD-RISC identified good resilience skills (median 29 [26–36]), whereas MBI highlighted significant values of DE (median 12 [7–17]), EX (median 24 [14–33]); EF was only slightly over-threshold (median 31 [26–36]). Our survey found increased use of sleep inducers in 13–15% of responders but no pathological insomnia (ISI median 10 [5–14]) (see Table 1; Table 2).

Risk factors associated with significantly worse scores were female gender (GAD-7, PCL C) (Table 3a); ages 31-40 y (ISI, CD-RISC, DE) (Table 3b); no stable partner (ISI, DE) (Table 3c); living in a flat (GAD-7, PHQ-9, EE, DE) (Table 3d); being a nurse or health care assistant (GAD-7, PCL C, PHQ-9, CD-RISC, ISI, DE) (Table 3e); length of service < 10 years (DE) (Table 3f); enduring mandatory job change (PCL C, PHQ-9) (Table 3g); having suffered a COVID-19 infection (GAD-7) (Table 3h); working in a COVID-19 department (GAD-7, ISI, PCL C, PHQ-9, DE) (Table 3i); and working in a different environment with increased intensity of care (GAD-7, PCL C, PHQ-9, ISI, DE) (Table 3j). In responders with a previous history of psychiatric disease, a higher level of depression was observed (Table 3k).

Using logistic regression, we found out that living in a flat (OR 2.27 [1.10-4.81]) and having to work in a high-intensity-of-care ward (2.83 [1.15-7.16]) were predictors of increased risk of anxiety (GAD-7) (Figure 1a); ages between 31-40 y (OR 2.8 [1.11-7.68]), being a nurse (OR 3.56 [1.59-8.36]) and having to work in a high-intensity-of-care ward (OR 8.43 [2.92-26.8]) were the strongest predictors of pathological stress (PCL-C) (Table 4; Figure 1b).

Eighty-seven professionals answered the phase 2 questionnaire; 120 (58%) questionnaires were lost at follow-up. For 30 more responders, we found incomplete answers or mistakes in reporting the matching identification code, thus we excluded these cases from the analysis. Comparing phase 1 and 2 questionnaires, we assessed 57 matches (28% response). Median scores on the psychological scales were uniformly improved, and we found a reduction in the percentage of responders scoring over the threshold, especially for anxiety, stress, and depression (Table 5; Figure 2).

Discussion

In our study, nearly half of HCWs showed psychological distress (anxiety, 50%; depression, 41%; posttraumatic stress, 66%; and insomnia, 30%). Nurses, women, and the youngest were more affected, together with the workers who were forced to change their jobs to increase the intensity of care or to work in COVID-19 departments; on the contrary, having a partner and living in a detached house were protective. Fortunately, 6 months later, all the psychological domains showed individual improvement.

Since February 2020, Italy has been strongly hit by the COVID-19 pandemic, which required a profound and rapid reorganization of the hospital system and the adoption of extraordinary restrictive rules to limit interaction and movement of the whole population.[3,4] HCWs experienced a high psychological burden in their professional and personal life, resulting in increased levels of anxiety, depression, insomnia, and distress.[5,6] The acute stress described by many authors at the end of the first COVID-19 wave,[16,18] resulting in burnout in 49-58% of HCWs, has probably changed to a chronic stress response still causing burnout in 38% of HCWs,[9,37,38] but also causing anxiety and depressive symptoms of a diverse entity. In our sample, psychological distress in any of the dimensions assessed was present in 40 to 66% of responders. Our results are in line with those of other Italian authors[9,10,15,21] and confirm the persistence of long-lasting occupational stressors[6,9,15,21] and of the COVID-19 impact on many psychological

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Table 1. Responders' characteristics described as (1) work related: working roles, education, seniority, workload; (2) personal situation and living situation; (3) individual physical and psychological condition; and (4) new symptoms, conditions, and changes in drug use related to COVID-19

Work-related covariates	Number of responders (percentage %)				
Working role	Doctor	96 (46%)			
	Nurse	91 (44%)			
	Heath-care assistant	12 (6%)			
	X-ray technician	6 (3%)			
	Administrative/ security	2 (1%)			
Academic degree	High school 39 (19%)	Graduation 168 (81%)			
Seniority	< 10 years 83 (40%)	> 10 years 124 (60%)	Median 15 [5-25]		
Work hours	< 40 h 62 (30%)	> 40 h 145 (70%)	Median 40 [36-45]		
Type of shift	Day shift 79 (38%)	2 shifts 14 (7%)	3 shifts 89 (43%)	Variable 25 (12%)	
Personal situation and living situation					
Marital status	Single	56 (27%)	Having a companion	151 (73%)	The companion is: 31% HCW
					43% other worker
					9% unoccupied
Living condition	Flat	137 (66%)	Independent house	70 (34%)	
	Cohabitants	None 25 (12%)	One 57 (27%)	Two or more 125 (60%)	
		Minor age 78 (37%)	Over 65 y 22 (11%)	Frail person 28 (13%)	
	Housekeeper support	93 (45%)	Increased in lockdown 32%	Unchanged 54%	Reduced 14%
Individual physical and psychological condition					
Physical condition	Poor 14%	Decent 36%	Normal 24%	Good 23%	Very good 3%
	Chronic illness	29%			
Psychological condition	Poor 18%	Decent 35%	Normal 22%	Good 18%	Very good 5%
History of previous psychiatric illness	7.5%				
COVID-19 infection	33%	More than 20 days isolation 53%	With moderate severe symptoms 17%		
COVID-19 infection in relatives	No 62%	Asymptomatic 5%	Mild 19%	Moderate 11%	Severe 8%
COVID-19 infection in cohabitants	No 73%	Asymptomatic 4%	Mild 21%	Moderate 6%	Severe 0.5%
New symptoms and conditions COVID-related					
New psychiatric diagnosis COVID-related	3 (1.5%)				
Increased substance use after COVID-19	Tobacco 14%	Alcohol 11%	Cannabis 1.5%	Psychiatric drugs 10%	Other drugs 3.5%
Altered nutrition	No variation 48%	Reduced appetite 13%	Increased appetite 19%	Binge eating 17%	Eating restrictions 3%
Therapy for insomnia	No 73%	Continuation 13%	New use 15% (70% due to COVID-19)		
Therapy for anxiety	No 82%	Continuation 5%	New use 13% (81% due to COVID-19)		
Psychiatric drugs	No 96%	Continuation 3%	New use 2% (60% due to COVID-19)		
Professional psychiatric care	No need 71%	Was not available 18%	Used 11% (9% for personal request, 1% routine work support)		
Perceived extra-working stress	Reduction 16 (8%)	No variation 50 (24%)	Increased 141 (68%)		
Having been exposed to stressors	Before COVID-19, 100 (48%)	After COVID-19, 107 (63%)			

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Table 2. Results to validated tools for evaluation of psychological distress

Validated score (cutoff threshold for clinical relevance)	Median, IQR	Subjects above threshold (number and percentage)
GAD-7 (8)	9 [5-14]	105 (50%)
PCL C (29)	42 [27-54]	139 (66%)
PHQ-9 (10)	9 [4-14]	85 (41%)
CD-RISC	29 [26-36]	NA
ISI (14)	10 [5-14]	52 (25%)
MBI, emotional exhaustion EX (> 23)	24 [14-33]	108 (52%)
MBI, depersonalization DE (> 8)	12 [7-17]	141 (68%)
MBI, fulfillment/professional efficacy EF (< 30)	31 [26-36]	81 (39%)

NA = not applicable. Median scores and interquartile range (IQR) are described, together with number of subjects over threshold for clinical relevance.

Table 3. Comparison of median [IQR] scores results in different groups

(3a)	Women (n = 154)	Men (n = 50)	Preferring not to answer (n = 3)	*P value*
GAD-7	10 [5-14]	7 [4-11]	13 [9-14.5]	***0.043***
PCL-C	44 [29.25-55]	33 [22-47.75]	51 [41-55]	***0.008***
PHQ-9	9.5 [4-14]	6 [3-12.75]	15 [8.5-17.50]	0.116
CD-RISC	29 [25- 31]	31 [27.5-33]	26 [19.5-30]	0.061
ISI	10 [5.25-15.0]	8 [4.25-13.0]	7 [4-10.5]	0.390
MBI, emotional exhaustion	25 [14-33.75]	21 [10.25-30]	26.50 [35-38]	0.180
MBI, depersonalization	12.5 [8.0-17]	11.5 [6-17]	13 [9.5-17]	0.765
MBI, fulfillment	31 [26-36]	32 [28-35]	29 [18.5-29.5]	0.350

(3b1) Age classes	21-30 (n = 44)	31-40 (n = 52)	41-50 (n = 53)	51-60 (n = 50)	61-70 (n = 8)	*P value*
GAD-7	7 [4-13]	10.5 [6.5-15]	9 [4.0-13.0]	9 [5.0-14.0]	6.5 [4-8.5]	0.367
PCL-C	37 [23-51]	47.5 [33.0-55]	38 [25.0-54]	45 [32.5-60.5]	35 [21.5-38.75]	0.064
PHQ-9	7.0 [3.75-11.25]	10.5 [7-15]	7 [3-15]	10 [5-14.75]	4.5 [3-8]	0.082
CD-RISC	30.0 [26.75-33.25]	27.5 [24.00-30.25]	30.0 [27.00-31.00]	30.0 [26.25-33.00]	31.5 [29.75-34.00]	0.019
ISI	8 [4-13]	11 [6.75-16]	9 [4-14]	10 [6.25-16.75]	6 [1.75-7.50]	0.029
MBI, emotional exhaustion	23.5 [10.75-31]	29.0 [19.50-35.75]	22.0 [12.00-31.00]	23.0 [17.00-31.75]	24.0 [8.25-31.75]	0.180
MBI, depersonalization	14 [7.5-18.25]	16 [11.75-19]	11 [7-17]	10 [6.00-13.75]	8 [7.50-13.25]	0.0005
MBI, fulfillment	33.0 [29.75-36]	29 [24-34]	30 [26-36]	31.5 [25.25-35.75]	35 [29.25-35.25]	0.203

(3b2)	31-40 y class (n = 52)	Others (n = 155)	*P value*
GAD-7	6.5 [10.5-15]	4.0 [8-13.5]	0.121
PCL-C	33.0 [47.5-55]	25.5 [40-53]	0.212
PHQ-9	7 [10.5-15]	4 [8-13.5]	0.066
CD-RISC	24 [27.5-30.25]	27 [30-33]	*0.003*
ISI	6.75 [11-16]	4.00 [9-14]	0.069
MBI, emotional exhaustion	19.5 [29-35.75]	12.0 [23-31]	*0.016*
MBI, depersonalization	11.75 [16-19]	6.00 [11-15.5]	*0.0003*
MBI, fulfillment	24 [29-34]	28 [32-36]	0.067

(3c)	Single (n = 38)	Divorced (n = 9)	With a partner (n = 56)	Separated (n = 9)	Married (n = 95)	*P value*
GAD-7	9 [5.25-11.75]	11 [7-15]	9.5 [5-14]	10 [3-14]	8 [5-13]	0.946
PCL-C	40.5 [31-50]	63 [41-67]	42.5 [25.75-53.25]	47 [33-65]	41 [27-52]	0.175
PHQ-9	9 [6-13]	17 [8-18]	9.6 [3.75-14]	12 [7-16]	8 [4-13]	0.291
CD-RISC	30 [25-32.75]	26 [23-30]	29 [26-32]	29 [28-30]	30 [26-32]	0.836
ISI	13 [7-16]	17 [10-20]	8.5 [4-13]	12 [8-15]	9 [4-12.5]	0.033

(*Continued*)

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Table 3. (*Continued*)

(3c)						
	Single (n = 38)	Divorced (n = 9)	With a partner (n = 56)	Separated (n = 9)	Married (n = 95)	*P value*
MBI, emotional exhaustion	23.5 [13.5-33.75]	33 [25-34]	24 [15.75-31]	20 [14-30]	24 [13-31.50]	0.830
MBI, depersonalization	14.5 [8.5-17.75]	14 [10-16]	14.5 [8.75-19]	12 [10-17]	10 [6-14.5]	0.027
MBI, fulfillment	32 [25-36]	27 [22-29]	31 [25.75-35]	30 [28-36]	32 [28-36.5]	0.331
(3d)						
	Living in a semi/detached house (n = 70)			Living in a flat (n = 137)		*P value*
GAD-7	13 [7-19]			14 [10-21]		*0.017*
PCL-C	37 [25-51]			43 [30-55]		*0.156*
PHQ-9	6.5 [4-11.75]			10 [4-15]		*0.057*
CD-RISC	30 [27-31.75]			29 [25-32]		*0.504*
ISI	8.5 [4.25-14.75]			10 [5-14]		*0.323*
MBI, emotional exhaustion	18.5 [11-30]			26 [16-34]		*0.006*
MBI, depersonalization	10 [6-15]			13 [8-18]		*0.006*
MBI, fulfillment	31 [27.25-37]			32 [26-35]		*0.436*
(3e)						
	Doctor (n = 85)	Nurse (n = 81)	Health care assistant (n = 12)	Radiology technician (n = 6)	Administrative (n = 2)	*P value*
GAD-7	7 [4-13]	11 [6-14]	10 [7.75-12.5]	7 [3-14.0]	2 [1.50-2.5]	*0.011*
PCL-C	36 [24-47]	50 [36-58]	44.5 [34.0-51.25]	39.5 [24.5-52.25]	20 [18.5-21.5]	*0.0002*
PHQ-9	7 [3-13]	11 [7-15]	8.5 [4.75-13.50]	7 [3.5-10.5]	3.5 [3.25-3.75]	*0.003*
CD-RISC	30 [27-33]	28 [25-30]	30.5 [28.75-32]	32 [30.25-33.75]	32.5 [29.75-35.25]	*0.020*
ISI	7 [3-11]	12 [7-16]	15 [7.75-18.25]	9 [7.25-13.75]	3 [3-3]	*0.0005*
MBI, emotional exhaustion	21 [13-33]	29.0 [17.0-34]	26.5 [15.5-32.5]	13.5 [10.0-25.25]	11.5 [8.75-14.25]	*0.107*
MBI, depersonalization	12 [7-17]	14 [9-18]	14 [10.25-17.5]	5 [5-5]	7 [4-10]	*0.026*
MBI, fulfillment	31 [27-35]	30 [25-36]	34.5 [26.25-37.25]	34.5 [32.25-37.5]	27.5 [25.75-29.25]	*0.580*
(3f)						
	Having worked less than 10 y			Having worked more than 10 y		*P value*
GAD-7	8.5 [5-13]			8.0 [4.75-14]		*0.733*
PCL-C	40.5 [27.25-51.75]			42.5 [26.75-54.00]		*0.559*
PHQ-9	9.0 [4-13.75]			8.0 [4.0-13.25]		*0.516*
CD-RISC	29 [25-32]			30 [30-40]		*0.604*
ISI	9.0 [4.25-13]			10 [4-15.25]		*0.586*
MBI, emotional exhaustion	24.5 [15-33.75]			23.5 [13-32.25]		*0.51*
MBI, depersonalization	15 [9.25-19]			11 [6-15]		*0.0005*
MBI, fulfillment	33 [27-36]			30 [25-36]		*0.40*
(3g)						
	No change (n = 124)		Involuntary change (n = 52)		Voluntary change (n = 19)	*P* value
GAD-7	8 [4.0 -13.25]		11 [6.0-15]		7 [6.5-12.5]	*0.128*
PCL-C	39 [23.75-51]		47.5 [36.75-58.25]		38. [31.5-51]	*0.018*
PHQ-9	7.5 [3-13]		12 [6-14]		7 [5-14]	*0.021*
CD-RISC	29.5 [25-33]		29 [26.75-31]		30.0 [25-31]	*0.6*
ISI	8 [3-14.0]		10 [6.75-15.0]		11 [7.50-13.5]	*0.178*
MBI, emotional exhaustion	23 [11.75-33.25]		29 [17-34.75]		23 [15-30]	*0.073*
MBI, depersonalization	12 [6-17]		13 [8.75-18]		13 [8.5-17]	*0.42*
MBI, fulfillment	31 [27-36]		31 [24.75-35.25]		32 [26.5-36.5]	*0.66*
(3h)						
	No COVID-19 infection (n = 131)			COVID-19-infected (n = 64)		*P value*
GAD-7	7 [4-13]			11 [5-15]		*0.047*
PCL-C	39 [24.5-51.0]			44 [30.0-57.25]		*0.066*
PHQ-9	7 [4.00-13.00]			10 [4.75-15.25]		*0.086*
CD-RISC	30 [26-33]			29 [25-31]		*0.155*

(*Continued*)

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Table 3. (*Continued*)

(3h)			
	No COVID-19 infection (n = 131)	COVID-19-infected (n = 64)	*P value*
ISI	8 [4-14.00]	11 [7-14.25]	*0.164*
MBI, emotional exhaustion	21 [13-32]	27 [15.75-34]	*0.27*
MBI, depersonalization	11 [7-17]	13.5 [6.75-17]	*0.48*
MBI, fulfillment	32 [27-35.5]	30.5 [26-36.0]	*0.64*
(3i)			
	No COVID-19 ward experience (n = 67)	COVID-19 ward experience (n = 128)	*P value*
GAD-7	5 [4-11]	10 [5-14]	*0.0004*
PCL-C	29.5 [21-44.5]	47 [32.75-55.5]	*0.000002*
PHQ-9	4.5 [3-9]	11 [5-15]	*0.000005*
CD-RISC	29 [25-32]	30 [26-32]	*0.932*
ISI	7 [3-10.75]	10 [6-15.25]	*0.0004*
MBI, emotional exhaustion	21 [12-32]	27 [15-33.25]	*0.086*
MBI, depersonalization	11 [6-14.75]	14 [8-18]	*0.005*
MBI, fulfillment	30.5 [28-35]	31.5 [25-36]	*0.990*
(3j)			
	No ward transfer (90)	Transfer without increasing intensity care (39)	Transfer with increasing intensity care (63)	*P value*
GAD-7	8 [4-13.75]	6 [3.5-11]	11 [7-15]	*0.004*
PCL-C	40.5 [24.25-52.5]	29 [23.5-49]	48 [36.5-56.5]	*0.0008*
PHQ-9	7.5 [3-13]	6 [3-10]	12 [7-15.5]	*0.0005*
CD-RISC	30 [25.25-33]	29 [25-31]	29 [26-31]	*0.53*
ISI	8 [3-14]	7 [3.5-11]	11 [8-16]	*0.01*
MBI, emotional exhaustion	23 [12-34]	18 [13.5-29.5]	29 [16-34]	*0.07*
MBI, depersonalization	11.5 [6-17]	11 [6-16]	14 [10-18]	*0.058*
MBI, fulfillment	31 [27.25-36]	32 [28-36]	31 [25-35]	*0.61*
(3k)			
	Previous psychiatric illness or therapy (n = 15)	No known previous psychiatric illness (n = 185)	*P value*
GAD-7	13 [10.5-15.5]	8 [5-13]	0.08
PCL-C	45 [36.5-63.5]	41 [26-52]	0.12
PHQ-9	18 [13-25]	8 [4-13]	*0.005*
CD-RISC	27 [21-31.5]	30 [26-32]	0.2
ISI	10 [7-13]	9 [4-14]	0.464
MBI, emotional exhaustion	29 [22-36]	23 [13-33]	0.08
MBI, depersonalization	13 [9-17]	12 [7-17]	0.7
MBI, fulfillment	31 [25.5-35]	32 [26-36]	0.58

Table 3, comparison among responders grouped by sex; 3b, comparison among responders grouped by age (b1) and comparison of the group of patients ages 30 to 40 years versus the other age groups (b2); 3c, comparison among responders grouped by marital status; 3d, comparison among responders grouped by living condition; 3e, comparison among responders grouped by working role; 3f, comparison among responders grouped by working seniority; 3g, comparison among responders grouped by change in work; 3h, comparison among responders grouped by having contracted COVID-19 infection; 3i, comparison among responders grouped by having worked in a COVID-19 ward; 3j, comparison among responders grouped by having changed their work (voluntary or involuntary); and 3k, comparison among responders grouped by having a previous psychiatric diagnosis.

different dimensions. Interestingly, we observed higher levels of anxiety and depressive symptoms compared with other Italian authors,[10,21] possibly showing a regional effect or merely due to differences in population selection and cutoffs.

We confirmed the importance of individual factors, like age and gender, in psychological distress and stress response. Female HCWs showed a higher level of anxiety and posttraumatic stress[9,10,21] probably because women are usually more affected by depression and anxiety in response to stressors,[9,10] and depression is strictly related to PTSD.[9,17,18,20] Women may have suffered more than their male colleagues with the pressure of working in the COVID-19 emergency, because of the Italian cultural traditional-bound double role of women in family care and house care; nevertheless, this trend was described also in different cultural settings.[18,39] Likewise, younger workers reported reduced resilience and more insomnia and depersonalization compared to their older colleagues with a great effect for the 30-40 age range. Other authors showed similar patterns for HCWs under age 40,[10,21] whereas others showed higher degrees of PTSD in older HCWs[9] or, on the contrary, a resilient pattern related to work seniority.[9,10,40] This last feature was observed also in our sample. We hypothesize the effect of additional extra-working stressors: Others had described the negative effect of life restrictions (lack of cultural, educational, recreational possibilities) that could have

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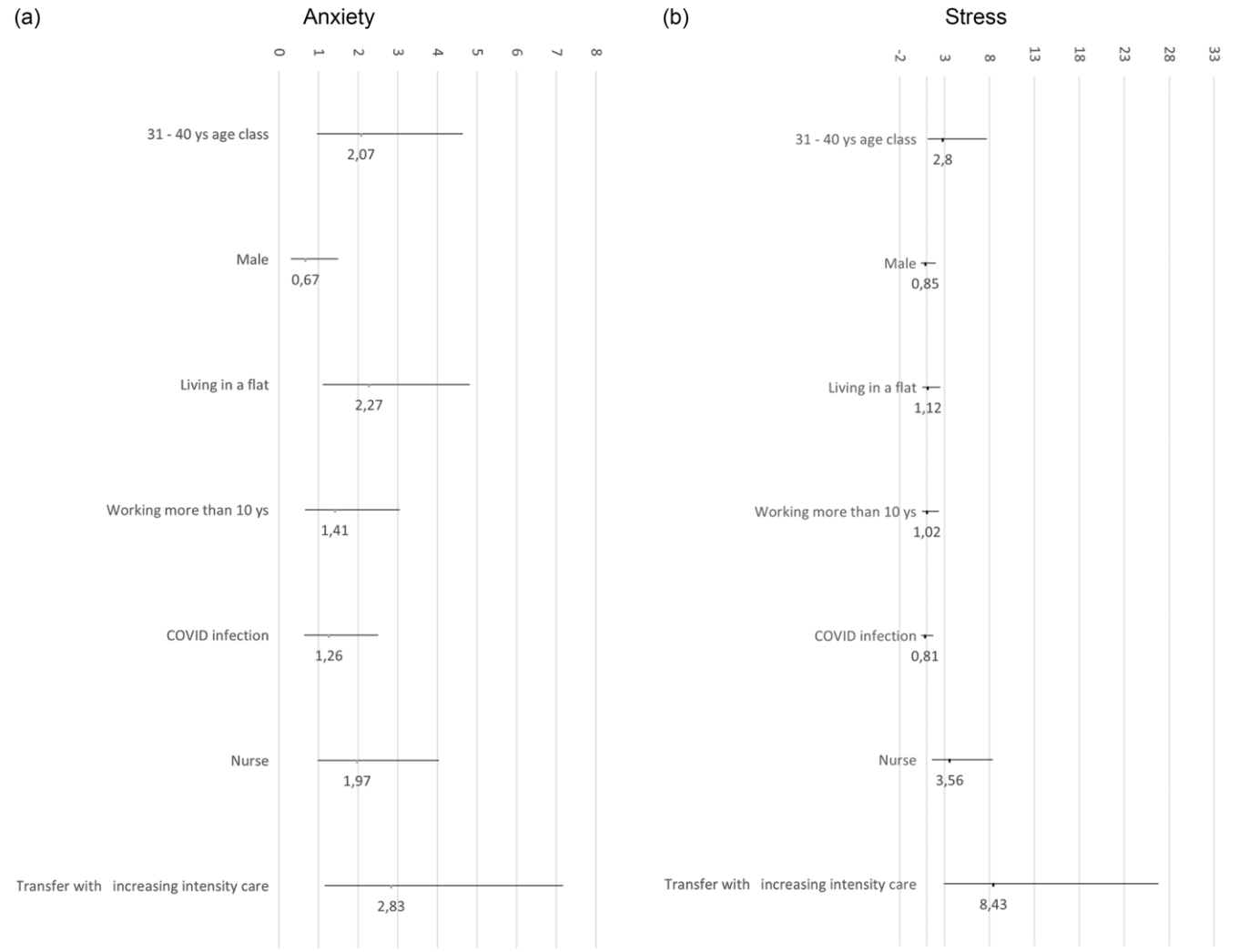

Figure 1. Logistic regression of factors associated with clinically relevant disease (score over threshold) for anxiety and stress. Odds ratio (OR) and 95% confidence intervals (CI). (a) Anxiety; (b) Stress.

had a greater impact on the age group 30-40 that is the most active in achieving personal life goals (work career, starting a family, and raising children, etc).[9,10,21] We confirmed the worse psychological burden on nurses as was previously observed after the first wave and proved in different cultural settings.[6,9,10,18,20,40] Interestingly, the same trend is shown also for health care assistants, who share similar exposure to stressors notwithstanding the differences in roles/responsibilities and whose psychological patterns are very similar, although rarely separately described in detail.[21,40]

In contrast with Collantoni et al.,[41] who showed a protective coping effect of teamwork in HCWs employed in COVID-19 units,[41] we highlighted that HCWs working in COVID-19 wards showed higher anxiety, depression, posttraumatic stress, insomnia, and depersonalization compared with those who worked in a regular ward. This feature was also described by other authors.[6,9,21,22] The fear of contagion, the lack of PPE and resources, and the emotional burden of assisting severely ill patients in isolation could have probably played a role in the first phase,[4,16–18] whereas, in the second phase fatigue treating COVID-19 patients and persistent need of working with full PPE,[17–19] despite a safer condition (HCW immunization) and more effective treatments, could have been determinants. Like other authors,[9,15,21,22] we observed that the ongoing need for involuntary displacement, associated with an increase in the level of care, had a role in causing anxiety, depression, insomnia, and, finally, burnout. Compared to what was observed in the first wave,[16,18] the fear of contagion seems to reduce over time, with only a higher level of anxiety persisting for those HCWs infected by COVID-19.

Interestingly, as previously observed by Ciulvica et al.,[10] living alone affects psychological well-being.[10] The relevance of loneliness as a contributor to mental health impairment was confirmed by previous studies showing its predictive role in the development and maintenance of depressive and anxiety symptoms,[42,43] but it was rarely evaluated.[10] Loneliness perception was possibly magnified by the change in the public opinion about the "heroes" of the first wave.[38] Moreover, personal living conditions are potent modifiers of personal coping capacity: in our population, anxiety and burnout were higher in HCWs living in a flat. This pattern could have been more evident in our sample because of the peripheral situation of our hospital, whose workers live in a suburban and countryside environment. Interestingly, similar findings were observed by Eggleton et al.[22] in a rural environment compared to an urban one; this feature was related to the different burden of cases.[22] The effect observed in our population is more probably

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Table 4. Logistic regression of factors associated with clinically relevant disease (score over threshold) for anxiety and stress. Odds ratio (OR) and 95% confidence intervals (CI)

Anxiety factors (GAD 7 > 8)	OR (CI: 2.5-97.5)	*P value*
31-40 y age class	2.07 (0.96-4.64)	*0.06*
Male	0.67 (0.30-1.49)	*0.33*
Living in a flat	2.27 (1.10-4.81)	***0.03***
Working more than 10 y	1.41 (0.66-3.04)	*0.37*
COVID-19 infection	1.26 (0.64-2.50)	*0.49*
Nurse	1.97 (0.98-4.038)	*0.058*
Transfer with increasing intensity care	2.83 (1.15-7.16)	***0.02***
Stress factors (PCL-C > 29)	**OR (CI: 2.5-97.5)**	***P value***
31-40 y age class	2.8 (1.11-7.68)	***0.03***
Male	0.85 (0.36-1.99)	*0.70*
Living in a flat	1.12 (0.50-2.50)	*0.76*
Working more than 10 y	1.02 (0.45-2.36)	*0.94*
COVID-19 infection	0.81 (0.37-1.76)	*0.6*
Nurse	3.56 (1.59-8.36)	***0.002***
Transfer with increasing intensity care	8.43 (2.92-26.8)	***0.0001***

Table 5. Comparison of individual median scores [IQR] and percentage of patients with clinically relevant symptoms (score over threshold) in responders at baseline (March 2021) and after 6 months (August 2021)

	Phase 1 (baseline)	Phase 2 (after 6months)	*P value*
GAD-7	11 [5-15]	7 [4-12]	***0.0002***
GAD-7 > 8	33 (58%)	24 (42%)	***0.04***
PCL-C	43 [30-58]	37 [24-50]	***0.000002***
PCL-C > 29	42 (74%)	32 (56%)	***0.02***
PHQ-9	10 [4-16]	6 [3-12]	***0.000008***
PHQ-9 > 10	27 (47%)	18 (31%)	***0.042***
CD-RISC	29 [24-31]	28 [25-32]	*0.797*
ISI	10 [4-15]	7 [5-12]	*0.057*
ISI > 14	15 (26%)	10 (18%)	*0.12*
MBI, emotional exhaustion	25 [16-35]	23 [15-31]	*0.108*
MBI, emotional exhaustion (> 23)	31 (54%)	28 (49%)	*0.28*
MBI, depersonalization	13 [8-17]	12 [8-17]	*0.953*
MBI, depersonalization (> 8)	42 (74%)	41 (72%)	*0.41*
MBI, fulfillment	29 (25-34)	30 [25-34]	*0.265*
MBI, fulfillment (< 30)	30 (53%)	25 (44%)	*0.17*

Wilcoxon test was used for paired data on 57 responders who completed the follow-up questionnaire.

suggestive of a resilience mechanism considering our high prevalence setting. It could be interesting to see whether these findings could be replicated in other suburban or countryside environments.

To our knowledge, this is one of the few longitudinal studies that followed the overtime changes in psychological distress, repeating HCW assessment after 6 months[6,23] to evaluate individual psychological changes and not only trends from repeated cross-sectional studies.[6,9]

Unfortunately, the rate of response to follow up was nearly 30%; this proportion, even lower than those observed by Rossi et al.,[23] suffers from the length of the questionnaire and from the distance from the beginning of the pandemic period. Indeed, we observed a very great number of studies on the mental health impact of COVID-19 in the immediate aftermath of the first wave, whereas only a few authors performed repeated studies at the beginning of 2021. Responders could have been already bored by the diffusion of many assessments via social media and professional associations. The first questionnaire was administered during the third Piedmont wave (the diffusion of the delta variant in our region), whereas the follow-up was administered 6 months later, after a quieter period during the summer season.

If the first evaluation was useful to highlight the persistence of long-term stressors and chronic effects 1 year after the beginning of the pandemic, the follow-up shows a general trend toward a reduction of the scores in nearly all dimensions, which is significant for anxiety, depression, and posttraumatic stress. These results are in line with Rossi et al.'s[23] study and probably could be explained by the improvement in the epidemiological situation, with a reduction of cases, return to prevalent care of non-COVID-19 patients,[18] and by the parallel lifting of life restrictions, with the beneficial effect of the holiday season.

The main strength of this study lies in its prospective design, which enables us to record how the perception of stress and the mental health of workers has evolved in relation to the following pandemic waves. The analysis of stress and mental health at various times of the pandemic and after its conclusion will help disentangle the effect of the epidemic from that of other common stressors in health care activities. This study, similarly to others,[6,9,10,15] documents the HCWs' mental health status, when the second wave had its effects and the fatigue of the first year of lockdown restrictions and of organizational emergency changes was more evident.[38] However, this study follows changes in HCWs' mental health after the end of the third wave, when the hope of extended immunization associated with the seasonal benefit lifted the psychological burden on HCWs.

Another strength is the choice to involve different HCWs, with various roles, not restricting the sample to intensivists, to doctors or nurses, or to frontline workers; in this way, our study can evaluate the effect of the contagion fear, of the rise in COVID-19 cases, other occupational stressors, and stressors that are common to the entire Piedmont population.[10] The comprehensive evaluation with many validated tools was another strength, although it was also a limitation because the length of the questionnaire reduced the participation rate and the follow-up rate.

Other limitations of this study are its observational nature, that methodology prevents cause-effect evaluation, the possible bias in reporting because of the self-administration of the questionnaire, and the low number of responders that was just above the estimated value for the minimum sample size and further reduced by the matching of cases in the second phase.

Due to the chronic and recurrent exposure to stressors in HCW population during emergencies and over time, prospective longitudinal studies are needed for a better understanding of HCW well-being. Further research should focus on screening tools that are useful to identify a subject at risk and evaluating effective interventions.

The extensive evidence of the different negative effects of the COVID-19 pandemic on the occupational well-being of HCWs should strengthen institutional and public awareness of the many potential challenges for these workers, not often surveyed with

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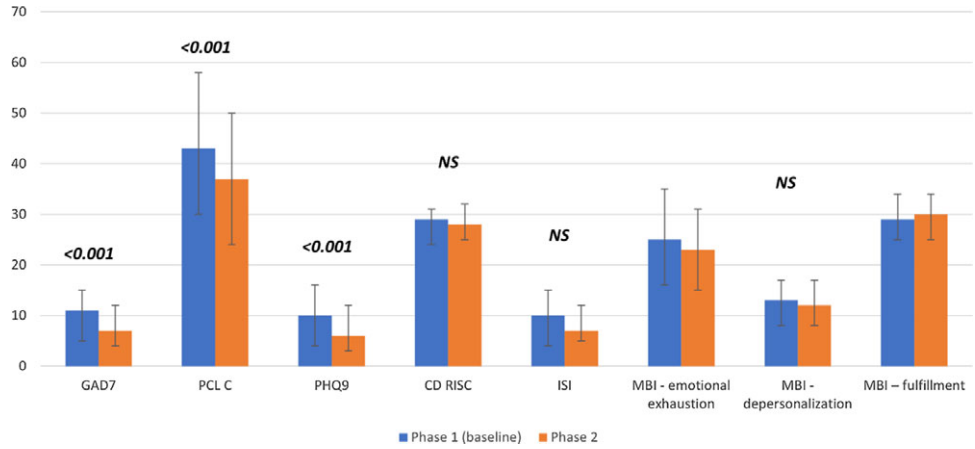

Figure 2. Comparison of individual median scores (IQR) in responders at baseline (March 2021 to phase1) and after 6 months (August 2021 to phase 2). Wilcoxon test for paired data on 57 responders who completed a follow-up questionnaire.

regard to mental health. The collected information could suggest how to monitor levels of exposure to stress factors with effective tools and should trigger organizational interventions at institutional and national levels to reduce psychosocial risk factors and to support their copying capacity.[44–47]

Conclusions

Psychological distress in HCWs has reached worrying levels and affects the quality of life and work activity. Nurses and health care assistants, women, and the youngest showed worse effects, in line with other published studies. Mandatory job change, increasing intensity of care when changing wards, COVID-19 department working experience, and being infected by COVID-19 were the most stressful factors. The presence of a partner and living in a detached house resulted to be protective. An improvement in all the psychological domains evaluated was observed 6 months after.

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Author contributions. VC, VG, GDS, AB, and GM conceived the study; VG and VC collected the data, managed the data, including quality control, and analyzed the data; VC drafted the manuscript; and all authors contributed substantially to its revision.

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