Three-Month Follow-up Study of Mental Health Outcomes After a National COVID-19 Lockdown:

Comparing Patients With Mood or Anxiety Disorders Living in an Area With a Higher Versus Lower Infection Incidence

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ABSTRACT

Objective: The COVID-19 pandemic and the related containment measures can represent a traumatic experience, particularly for populations living in high incidence areas and individuals with mental disorders. The aim of this study was to prospectively examine posttraumatic stress disorder (PTSD), anxiety, and depressive symptoms since the end of the first COVID-19 pandemic wave and Italy's national lockdown in subjects with mood or anxiety disorders living in 2 regions with increasing pandemic incidence.

Methods: 102 subjects with a *DSM-5* anxiety or mood disorder were enrolled from June to July 2020 and assessed at baseline (T0) and after 3 months (T1) with the Impact of Event Scale-Revised, Patient Health Questionnaire-9, Generalized Anxiety Disorder 7-Item, and Work and Social Adjustment Scale. At T1, subjects were also assessed by means of the Trauma and Loss Spectrum Self-Report for PTSD.

Results: At T0, subjects from the high COVID-19 incidence area showed higher levels of traumatic symptoms than those from the low COVID-19 incidence area ($P < .001$), with a decrease at T1 with respect to T0 ($P = .001$). Full or partial *DSM-5* PTSD related to the COVID-19 pandemic emerged in 23 subjects (53.5%) from the high COVID-19 incidence area and in 9 (18.0%) from the low COVID-19 incidence area ($P < .001$).

Conclusions: Subjects with mood or anxiety disorders presented relevant rates of PTSD, depressive, and anxiety symptoms in the aftermath of the lockdown, and in most cases these persisted after 3 months. The level of exposure to the pandemic emerged as a major risk factor for PTSD development. Further long-term studies are needed to follow up the course of traumatic burden.

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Coronavirus disease 2019 (COVID-19), declared a pandemic on March 11, 2020, by the World Health Organization, rapidly spread from China and caused pervasive lifestyle changes worldwide. Italy was the second large country after China to undergo a severe diffusion of the contagion and the first Western country forced to adopt, on March 9, 2020, a strict lockdown extended to the entire nation. After 55 days of national lockdown, the number of COVID-19 cases exceeded 200,000 and the death count 31,000, while most of the population was living in home-confinement environments, avoiding social interactions.[1] From May 4, 2020, there has been a gradual reopening of financial and commercial activities (the so-called "phase 2" of the national health emergency) throughout the country.

The COVID-19 pandemic and the related containment measures adopted in the acute phase, such as quarantine or social distancing, could have represented a traumatic experience affecting the mental health and well-being of the general population,[2–8] health care workers,[9–11] COVID-19 survivors,[12] and people with mental disorders.[13–15] In this regard, it has been suggested,[16–20] although not univocally,[21,22] that people affected by mental disorders are more vulnerable to the development of posttraumatic stress disorder (PTSD), depressive, and anxiety symptoms.

This notwithstanding, it should be considered that studies of the impact of COVID-19 pandemic on people affected by mental disorders are still scarce and that the majority of them share similar limitations, such as the cross-sectional design, online self-report assessment, self-report diagnosis, and snowball sampling.[7,14,17,22–24] Moreover, to the best of our knowledge, scant data are available on the midterm effects of the COVID-19 pandemic and lockdown measures on the mental health of individuals with mental disorders. Interestingly, only a few clinical studies in such a population have been conducted in the framework of the COVID-19 pandemic.[17,25] Some authors[17,26] found a worsening of psychiatric conditions in a considerable percentage of subjects with preexisting anxiety or mood disorders. Specifically, it has been suggested[15,26–28] that people with a previous history of anxiety or mood disorders are particularly prone to experiencing an adverse emotional impact of the COVID-19 pandemic, related to the fear of contagion and the lockdown-related changes in work activities and lifestyle. These subjects are at increased risk of COVID-19 infection[29] and may develop more severe forms of the disease when infected.[20] Thus,

Clinical Points

- Only a few clinical studies of subjects affected by mood and anxiety disorders have been conducted in the context of the COVID-19 pandemic.
- Subjects living in an area with high levels of COVID-19 infection exposure tend to develop posttraumatic symptoms and PTSD, suggesting the need for tailored supportive strategies and treatment to prevent and address PTSD.
- Clinicians should systematically assess PTSD symptoms in vulnerable populations, such as those affected by mental disorders, across the pandemic waves, particularly in the areas most affected by the pandemic. The increasing use of telehealth services during such periods will possibly reduce the hazard of person-to-person exposure and allow continuous follow-up of patients.

it could contribute to the worsening of psychiatric symptoms and/or an increased recurrence rate besides the onset of possible posttraumatic stress reactions.[14,30,31] However, these findings are not univocal, since other studies found minimal, if any, worsening in symptomatology.[21,22,32]

Furthermore, despite the evidence of the role of differential degree of exposure to the pandemic in the genesis of COVID-19 pandemic–related PTSD symptoms,[33,34] to the best of our knowledge, no study has examined whether living in areas with different intensities of outbreak could determine different effects on the mental health of subjects with mood and anxiety disorders. As for many other countries, the rate of incidence of COVID-19 infection in different areas of Italy was very dissimilar while the containment measures and the economic consequences were uniform across the country. For instance, epidemiologic data from governmental sources reported 18,845 COVID-19 cases with 1,743 deaths during the national lockdown in Veneto (northeastern Italy), a region with a high level of exposure.[35] On the other hand, an area with a lower level of exposure, Tuscany (central Italy), presented 9,859 cases and 973 deaths.[35] Consequently, the burden on the health care system and the perceived threat in the general population were unequally distributed too. Of note is that some data suggest that living in an area with a high impact of the outbreak might be considered as a proximity risk factor for developing PTSD symptoms,[36] as previously highlighted in a study investigating posttraumatic stress symptoms developed in the aftermath of an earthquake.[37] Finally, other recognized risk factors for PTSD symptoms, such as female gender and age,[38–41] have still been little explored among people with mental disorders.[12,34,36,42]

The present naturalistic study, conducted at the end of Italy's first national COVID-19 lockdown phase, examined, for the first time, the effect of COVID-19 outbreak intensity on the presence and magnitude of posttraumatic stress, anxiety, and depression symptoms in a sample of subjects with mood or anxiety disorders who were treated in 2 outpatient clinics in areas with differing infection incidence. Specifically, our aim was to investigate whether subjects living in a high incidence area presented higher levels of anxiety, depressive, and traumatic symptoms, besides lower levels of functioning, than those living in a low incidence area. Moreover, the same subjects were assessed again after 3 months from baseline to evaluate (1) the change that occurred across these symptoms over time and (2) the development of posttraumatic stress symptoms and/or disorder and their associated risk factors.

METHODS

Study Sample

The present naturalistic prospective cohort study included a sample of 102 subjects (51 [50%] males and 51 [50%] females) with a current *DSM-5* diagnosis of anxiety disorder (21 [20.6%]), major depressive disorder (40 [39.2%]), or bipolar disorder (41 [40.2%]). Subjects were consecutively offered participation from June 1–July 30, 2020, in the immediate aftermath of the so-called first wave of the COVID-19 pandemic in Italy and of the related national lockdown. All patients seeking a first or follow-up psychiatric visit were recruited at the outpatient psychiatric services of 2 major Italian university hospitals located in 2 regions exposed at increasing COVID-19 pandemic incidence: Pisa (Tuscany region, central Italy), referred to as the "low COVID-19 incidence area," and Verona (Veneto region, northeastern Italy), referred to as the "high COVID-19 incidence area." The rate of participation was 92.73%. Subjects who declined to participate in the study did not differ with respect to those who participated in terms of age, gender, psychiatric diagnosis, or incidence area. Exclusion criteria included age < 18 years, intellectual disabilities, and other limits to correctly understanding and completing the questionnaires. Three (2.9%) of the enrolled subjects presented a first psychiatric episode, while the others (N = 99, 97.1%) reported the recurrence of a preexisting mental disorder. Furthermore, all subjects with a diagnosis of bipolar disorder reported a depressive episode at the time of enrollment. All subjects were assessed at the time of enrollment in the study (T0) and after 3 months (T1), and both evaluations were performed in the framework of a routine psychiatric visit. During the study period, all subjects were in an outpatient treatment program characterized by periodic psychiatric visits with psychopharmacologic treatment, based on physician clinical judgment, as well as a psychological intervention consisting of nonstructured individual support sessions.

All participants provided written informed consent after receiving a detailed description of the study. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Area Vasta Nord-Ovest Toscana (n. 17152/2020) and of the Provinces of Verona and Rovigo (n. 26045/2020).

Instruments and Assessments

At baseline (T0), all participants were diagnosed using the Structured Clinical Interview for *DSM-5* Disorders (SCID-5)[43] and were asked to complete the following assessments:

Impact of Event Scale-Revised (IES-R)[44] for posttraumatic stress symptoms, Patient Health Questionnaire-9 (PHQ-9)[45] for depressive symptoms, Generalized Anxiety Disorder 7-Item (GAD-7)[46] for anxiety symptoms, and Work and Social Adjustment Scale (WSAS)[47] for global impairment in functioning related to mental health burden. At follow-up (T1), all participants were asked to complete these instruments again and, for the first time, to complete the Trauma and Loss Spectrum Self-Report (TALS-SR),[48] to assess symptomatological PTSD. Data on social, demographic, and COVID-19 pandemic were collected from each participant.

The IES-R is a 22-item scale measuring PTSD symptoms in the last week. Items are divided in 3 subscales: intrusion, avoidance, and hyperarousal. The mean score of the items of each subscale determines the subscale score, while the sum of each item represents the total score. The Italian version of the scale was validated and shows good internal consistency.[44] In accordance with the aim of the study, the items referred to the traumatic events that the subjects had experienced in the framework of the COVID-19 pandemic.

The PHQ-9 is one of the most-used self-assessment tools for the screening of depressive symptoms. It consists of 9 items that investigate the presence of depressive symptoms in the last 2 weeks, each evaluated on a scale of 0 (never) at 3 (almost every day). The sum of each item determines the total score. PHQ-9 internal consistency and test-retest reliability of the Italian version were high.[45]

The GAD-7 is a self-assessment questionnaire used as a tool for screening and measuring anxious symptoms. Particularly, it investigates the frequency of anxious symptoms in the last 2 weeks using 7-item with a score ranging from 0 (never) to 3 (almost every day).

The TALS-SR includes 116 items exploring a range of loss and/or traumatic events, besides symptoms or behaviors that could represent manifestations of a stress response syndrome. Subjects were asked to complete the scale referring to potentially traumatic events related to the COVID-19 pandemic. Item responses are coded in a dichotomous way (yes/no). The instrument is organized into 9 domains: loss events (I), grief reactions (II), potentially traumatic events (III), reactions to losses or upsetting events (IV), re-experiencing (V), avoidance and numbing (VI), maladaptive coping (VII), arousal (VIII), and personal characteristics/risk factors (IX). In accordance with previous studies,[41,49] the presence of PTSD was assessed by means of TALS-SR items endorsed corresponding to *DSM-5* criteria for PTSD diagnosis. Specifically, we utilized the following matching between symptom criteria and TALS-SR items:

- Criterion B, "intrusion symptoms" (B1 = 80, B2 = 77, B3 = 79, B4 = 78, B5 = 81);
- Criterion C, "avoidance" (C1 = 86, C2 = 87 and/or 88 and/or 89);
- Criterion D, "negative alterations in cognitions and mood" (D1 = 90, D2 = 95, D3 = 85, D4 = 96, D5 = 91, D6 = 93, D7 = 92);
- Criterion E, "alterations in arousal" (E1 = 108, E2 = 99 and/or 100 and/or 102 and/or 103 and/or 104, E3 = 106, E4 = 107, E5 = 105, E6 = 109).

A partial symptomatological PTSD diagnosis[50] was assessed according to meeting 2 or 3 of the *DSM-5* PTSD criteria B, C, D, and E. The validated Italian version of the TALS-SR showed good intraclass correlation and good internal consistency.[48]

The WSAS is a 5-item self-assessment questionnaire used to evaluate how work and social adjustment was affected in the week prior to the assessment. Each of the 5 items is rated on a 9-point scale ranging from 0 (not at all) to 8 (severe interference), so that the total scores are between 0 and 40. The internal consistency of the instrument varies from 0.70 to 0.94, and the test-retest reliability is 0.73.[47]

Statistical Analyses

Descriptive statistics are reported by frequencies and percentages for categorical variables and means (standard deviations) for continuous variables. Comparisons between low and high COVID-19 incidence area were performed with χ^2 tests in the case of categorical variables and *t* tests for independent groups in the case of continuous variables. A 2-way analysis of variance (ANOVA) was run to examine the effect of center and time on each clinical assessment. Changes between baseline and follow-up in clinical assessments within each center were evaluated by *t* test for paired groups. To explore the association between PTSD (partial/full) and living in a high COVID-19 incidence area, a logistic regression model was estimated, adjusted for gender (female), age (above 50 years), and being concerned about COVID-19–related consequences (in terms of health and/or job). All tests were bilateral at $P < .05$. All analyses were performed by Stata 17 for Windows.

RESULTS

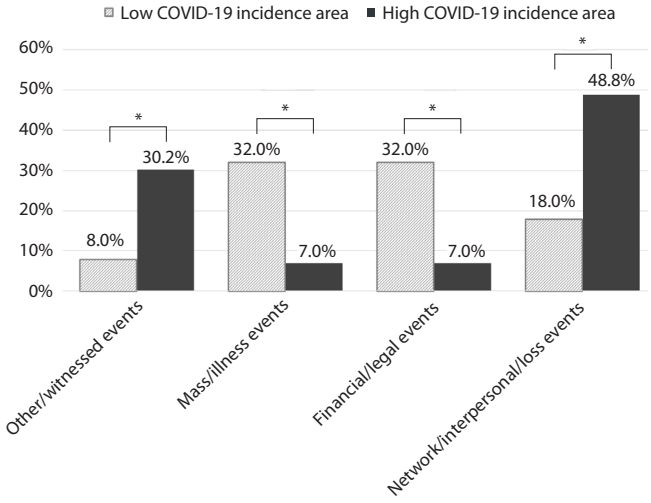
A total of 50 subjects (49.0%, age: mean [SD] = 47.5 [15.0] years; range, 20–74 years) were consecutively enrolled from the high COVID-19 incidence area and 52 (51.0%, age: mean [SD] = 49.0 [16.3] years; range, 19–73 years) from the low COVID-19 incidence area. Subjects from the high COVID-19 incidence area were significantly more represented by males ($P < .001$), had more severe concerns about the COVID-19 pandemic ($P < .001$), and had a higher likelihood of being quarantined or positive for SARS-COV-2 ($P = .051$) with respect to those from the low COVID-19 incidence area. Three subjects from the high COVID-19 incidence area reported being positive for COVID-19 and developing paucisymptomatic disease. No one was hospitalized due to COVID-19. Details on sociodemographic variables are summarized in Table 1, and rates of potentially traumatic events experienced by subjects from the 2 areas are reported in Figure 1. Furthermore, subjects from the high COVID-19 incidence area showed higher IES-R subscales and total mean scores than those from the low COVID-19 incidence

Table 1. Comparison of Patients' Sociodemographic, Clinical, and COVID-19–Related Characteristics Between Low and High COVID-19 Incidence Areas[a]

Characteristic	Low COVID-19 incidence area (N = 52)	High COVID-19 incidence Area (N = 50)	*P* value χ^2 test or independent *t* test
Gender			
Female	35 (67.3)	16 (32.0)	<.001
Male	17 (32.7)	34 (68.0)	
Age, mean (SD), y	49.0 (16.3)	47.5 (15.0)[b]	.368
Marital status			
Married	20 (38.5)	25 (50.0)	.491
Single	17 (32.7)	14 (28.0)	
Divorced/widowed	15 (28.8)	11 (22.0)	
Education			
Primary school	20 (38.5)	19 (40.4)	.646
Secondary school	23 (44.2)	17 (36.2)	
University degree	9 (17.3)	11 (23.4)	
Employment			
Employed	20 (38.5)	29 (58.0)	.102
Unemployed	13 (25.0)	11 (22.0)	
Other condition	19 (36.5)	10 (20.0)	
Medical comorbidities			
Yes	32 (61.5)	34 (68.0)	.634
No	20 (38.5)	16 (32.0)	
Psychiatric diagnosis			
Anxiety disorder	8 (15.4)	13 (26.0)	.309
Major depressive disorder	20 (38.5)	20 (40.0)	
Bipolar disorder	24 (46.2)	17 (34.0)	
Psychiatric family history			
No	6 (11.5)	46 (88.5)	<.001
Yes	32 (65.3)	17 (34.7)	
Financial difficulties due to lockdown			
Yes	7 (14.6)	9 (18.8)	.584
No	41 (85.4)	39 (81.3)	
Having been in quarantine or positive for COVID-19			
Yes	5 (9.6)	12 (24.0)	.051
No	47 (90.4)	38 (76.0)	
Having been in quarantine			
Yes	5 (9.6)	12 (24.0)	.092
No	47 (90.4)	38 (76.0)	
Having been positive for COVID-19			
Yes	0 (0.0)	3 (6.0)	.228
No	52 (100.0)	47 (94.0)	
At least 1 relative/close friend with a COVID-19–related condition			
Yes	6 (11.5)	9 (18.0)	.357
No	46 (88.5)	41 (82.0)	
Severe concerns about COVID-19			
Yes	16 (33.3)	41 (97.6)	<.001
No	32 (66.7)	1 (2.4)	

[a]Values expressed as N (%) unless otherwise noted.
[b]Data missing for 4 patients.

Figure 1. Comparison of Rates of Potentially Traumatic Events Between Low and High COVID-19 Incidence Areas



*$P < .05$.

Table 2. Comparison of Patients' Clinical Assessments at Baseline (T0) (GAD-7, PHQ-9, IES-R, and WSAS) Between Low and High COVID-19 Incidence Areas

Clinical assessment at T0	Low COVID-19 incidence area (N = 52), mean (SD)	High COVID-19 incidence area (N = 50), mean (SD)	*P* value independent *t* test
GAD-7	8.31 (4.68)	8.68 (5.37)	.709
PHQ-9	10.20 (5.96)[a]	8.42 (5.11)	.111
IES-R			
Total	11.58 (14.73)	28.04 (17.10)[a]	<.001
Intrusion	0.50 (0.66)	1.08 (0.80)[a]	<.001
Avoidance	0.49 (0.73)	1.42 (0.84)[a]	<.001
Arousal	0.60 (0.78)	1.34 (0.96)[a]	<.001
WSAS	12.25 (9.44)[a]	11.68 (8.68)	.752

[a]Data missing for 1 patient.
Abbreviations: GAD-7 = Generalized Anxiety Disorder 7-Item, IES-R = Impact of Event Scale-Revised, PHQ-9 = Patient Health Questionnaire-9, WSAS = Work and Social Adjustment Scale.

area at baseline observation (T0) (mean [SD] = 28.04 [17.10] vs mean [SD] = 11.58 [14.73], $P < .001$). Details on the clinical variables at T0 are shown in Table 2.

Among the subjects enrolled, 92 (90.2%) completed the 3-month follow-up (T1), whereas 10 subjects (9.8%), 2 from the center at the lower exposure level and 8 from the center at the higher exposure level, dropped out. At both centers, dropouts were related to the fact that subjects interrupted follow-up visits and avoided routine visits at the hospital centers to which they were referred, despite being phone contacts, due to the fear of contagion.

By running a 2-way ANOVA with each clinical assessment as dependent variable and area and time as factors, a significant interaction between the effects of area and time was found for IES-R total and subscales (*F* test, $P < .001$) and WSAS (*F* test, $P < .001$) (data available from the authors on request). In detail, subjects from the high COVID-19 incidence area exhibited a significant decrease in the IES-R subscales and total mean scores at T1 with respect to T0 ($P = .001$). Conversely, subjects from the low COVID-19 incidence area reported a statistically significant increase in the WSAS total mean score at T1 with respect to T0 ($P = .002$). Changes in the clinical assessments between T0 and T1 within each group are described in Table 3.

Regarding the TALS-SR, 38.0% of subjects enrolled from the high COVID-19 incidence area and 19.2% of those from the low COVID-19 incidence area reported at least a loss

Table 3. Changes in Patients' Clinical Assessments (GAD-7, PHQ-9, IES-R, and WSAS) Between Baseline (T0) and Follow-up (T1) Within Each Sample Living in the Low Versus High COVID-19 Incidence Area

	Low COVID-19 incidence area (N = 50)[a]			High COVID-19 incidence area (N = 42)[b]		
Clinical assessment	T0, mean (SD)	T1, mean (SD)	*P* value repeated *t* test	T0, mean (SD)	T1, mean (SD)	*P* value repeated *t* test
GAD-7	8.32 (4.77)	10.20 (5.97)	.051	8.64 (5.63)	7.38 (5.19)	.103
PHQ-9	10.18 (6.08)	10.24 (6.88)	.947	8.43 (5.37)	6.64 (8.21)	.102
IES-R	12.04 (14.84)	12.18 (16.28)	.956	28.10 (16.57)	18.76 (15.27)	.001
Intrusion	0.52 (0.66)	0.54 (0.76)	.891	1.08 (0.80)	0.76 (0.86)	.009
Avoidance	0.51 (0.73)	0.49 (0.76)	.863	1.44 (0.78)	0.85 (0.63)	.040
Arousal	0.63 (0.79)	0.65 (0.84)	.840	1.32 (0.97)	0.98 (0.85)	.002
WSAS	12.22 (9.61)	17.45 (9.02)	.002	11.43 (9.13)	9.76 (8.70)	.131

[a]Data missing for 2 patients at follow-up.
[b]Data missing for 8 patients at follow-up.
Abbreviations: GAD-7 = Generalized Anxiety Disorder 7-Item, IES-R = Impact of Event Scale-Revised, PHQ-9 = Patient Health Questionnaire-9, WSAS = Work and Social Adjustment Scale.

Table 4. Comparisons of Patients' TALS-SR Domains at Follow-up (T1) and *DSM-5* PTSD Criteria Between Low and High COVID-19 Incidence Areas

	Low COVID-19 incidence area (N = 50),[a]	High COVID-19 incidence area (N = 43)[b]	*P* value
TALS-SR domains at T1, mean (SD)			Independent *t* test
I. Loss events	0.20 (0.58) (1 missing)	0.35 (0.65)	.261
II. Grief reactions	7.67 (3.83) (2 missing; 42 NA)	9.00 (5.17) (31 NA)	.586
III. Potentially traumatic events	1.35 (2.55) (1 missing)	1.32 (1.47) (3 missing)	.947
IV. Reaction to losses and/or potentially traumatic events	2.04 (2.75)	4.91 (4.35)	<.001
V. Reexperiencing	0.58 (1.16)	1.91 (2.29)	.001
VI. Avoidance and numbing	0.54 (1.18)	2.33 (2.61)	<.001
VII. Maladaptive coping	0.36 (0.94)	0.37 (0.82)	.948
VIII. Arousal symptoms	0.90 (1.37)	1.67 (1.77)	.020
DSM-5 criteria for PTSD, N (%)			χ^2 test
No	41 (82.0)	20 (46.5)	<.001
Partial/full	9 (18.0)	23 (53.5)	

[a]Two missing at T1.
[b]Seven missing at T1.
Abbreviations: NA = not applicable, PTSD = posttraumatic stress disorder, TALS-SR = Trauma and Loss Spectrum Self-Report.

event, while 61.0% of subjects enrolled from the high COVID-19 incidence area and 57.1% of those from the low COVID-19 incidence area reported at least 1 potentially traumatic event. A full or partial *DSM-5* PTSD diagnosis emerged in 23 subjects (53.5%) from the high COVID-19 incidence area and in 9 subjects (18.0%) from the low COVID-19 incidence area ($P < .001$). In particular, subjects enrolled from the high COVID-19 incidence area reported significantly higher scores than those enrolled from the low COVID-19 incidence area in the following TALS-SR domains: reactions to losses or upsetting events (IV), reexperiencing (V), avoidance and numbing (VI), and arousal (VIII) (see Table 4).

Living in a high COVID-19 incidence area was found to be a risk factor for at least partial PTSD (OR = 3.4; 95% CI, 1.1–9.9; $P = .027$), by adjusting for female gender (OR = 1.0; 95% CI, 0.4–2.8; $P = .975$), age above 50 years (OR = 0.6; 95% CI, 0.2–1.6; $P = .327$), and being concerned about COVID-related consequences (OR = 3.6; 95% CI, 1.1–12.5; $P = .044$).

DISCUSSION

To the best of our knowledge, this is the first naturalistic longitudinal study aimed at evaluating the prevalence and magnitude of posttraumatic stress, anxiety, and depressive symptoms among subjects suffering from mood or anxiety disorders treated in 2 outpatient clinics in Italy at the end of the COVID-19 pandemic first wave and exposed at different intensity of outbreak.

Patients living in a high COVID-19 incidence area showed significantly higher levels of PTSD symptoms with respect to those from a low COVID-19 incidence area in the immediate aftermath of a national lockdown. Further, PTSD symptoms significantly decreased after 3 months among subjects living in the most exposed area, despite their still showing statistically significantly higher rates of full/partial PTSD and PTSD symptoms, with respect to patients living in an area with a lower incidence of contagion. Living in a high COVID-19 incidence area was found to be a risk factor for full or partial PTSD, adjusting for female gender, age, and being concerned about COVID-19–related consequences.

The present findings are in line with evidence suggesting a dose-response effect in PTSD, with increased trauma exposure leading to higher levels of stress-related psychopathology.[37,51–55] In the context of exposure to natural disasters, significantly higher PTSD rates were reported in individuals living in more damaged areas.[37,51,54] Similarly, studies conducted during previous outbreaks of infectious diseases pointed out that level of exposure might be identified as a significant predictor for posttraumatic stress reactions.[10,53,55,56] Increasing evidence has also emerged in the framework of the COVID-19 outbreak. Tang and colleagues[33] found, in a large sample of home-quarantined college students, that living in severely afflicted areas was a significant risk factor for

psychological distress. Data from a large survey of the Chinese population corroborate these findings.[34] Online surveys of the general population in Italy reported lower rates of severe acute stress symptoms or PTSD than those found in our study, ranging from 4.3% to 27.5%.[2,57,58] However, it is difficult to compare results for the relevant methodological differences across studies because ours is a naturalistic prospective cohort study. In this context, our results increase the existing, still insufficient, knowledge on the traumatic burden among patients affected by mental disorders in the ongoing pandemic.[59] Subjects with mental disorders living in an area with high levels of exposure tend to develop traumatic distress more frequently than those living in an area with lower levels of exposure, suggesting the need for tailored supportive strategies and treatment to prevent and address PTSD.

Notably, the changes that occurred in subjects' clinical assessments between baseline and follow-up within each group living in high versus low COVID-19 incidence areas pointed to different trends. In detail, these data highlight the increased burden of PTSD symptoms at baseline in the first group, in the aftermath of the national lockdown, with reduction of symptoms at follow-up. However, even at the 3-month follow-up, subjects from the high COVID-19 incidence area showed higher rates of PTSD than those from the low incidence areas. Long-term studies are still needed to evaluate possible delayed consequences of the COVID-19 pandemic.

No differences emerged in depressive and anxiety symptoms, besides impairment in functioning, between the two groups at baseline. These results confirm previous findings suggesting that, in subjects with mood or anxiety disorders, life-impacting changes resulting from home-confinement environments and social isolation could reexacerbate psychiatric symptoms per se, regardless of the level of outbreak exposure.[15,16,59–61]

When considering the results of the present study, major strengths and limitations should be noted. Regarding strengths, we argue that the sample, despite its limited size, is representative of the clinical population of clinical outpatient services at the time of the first COVID-19–related national lockdown. Furthermore, the sample was consecutively recruited, with no major patient selection bias, and was assessed longitudinally, with follow-up visits performed at 3 months. In this regard, dropout rates were not relevant despite the fact that most of the patients lost to follow-up reported refusal to access hospitals or outpatient clinics because of fear of contagion. Finally, all subjects were evaluated by means of *DSM-5* assessment diagnoses.

Regarding the limitations, we note the following: the limited sample size and diagnoses included, which may impact a possible in-depth analysis of the predictors of PTSD development, and the inclusion of only outpatients from major psychiatric clinics. Consequently, the present sample could be considered a convenience sample that might not be representative of all individuals in the community. Another limitation was the use of self-report instruments, with respect to clinical interviews, to assess posttraumatic stress, depressive, and anxiety symptoms. Finally, it is important to recall the country-specific circumstances related to the COVID-19 pandemic in which the study was developed, not only the geographical context but also the stage of the COVID pandemic that was considered, which may limit the generalizability of the results. However, this limitation is mitigated by the fact that patients were recruited in the context of routine psychiatric visits and assessed by trained clinicians in a longitudinal study design.

In conclusion, patients with mood or anxiety disorders presented relevant rates of PTSD, depressive, and anxiety symptoms in the aftermath of the national lockdown related to the COVID-19 pandemic. Most of these symptoms did not decrease during the first 3 months, suggesting the presence of prolonged psychopathological reaction to the COVID-19 pandemic. Furthermore, we found a robust effect of level of exposure to the pandemic as a major risk factor for PTSD development. This finding highlights the unmet needs for health care in the vulnerable psychiatric population, suggesting that clinicians should systematically assess PTSD symptoms in the aftermath of lockdowns and across the pandemic waves, particularly in the most affected areas. We believe that the increasing use of telehealth services in such periods will possibly reduce the hazard of person-to-person exposure and allow continuous follow-up of patients.[16,62,63] Long-term studies are, however, warranted to examine the course of traumatic burden over time and the impact of targeted health care strategies also extended to other psychiatric diagnoses.

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