

Longitudinal trajectories of anxiety and depression in subjects with different mental disorders after one year in the COVID-19 pandemic

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ABSTRACT

The aim of this study was to prospectively assess the development and trajectories of anxiety and depressive symptoms among subjects with different mental disorders, during the 3rd wave of the COVID-19 pandemic (T0, March-April 2021) while strict containment measures were applied in Italy, and after 3 months (T1, June-July 2021), with reduced restrictive measures. A sample of 527 subjects, with different DSM-5 diagnoses, was enrolled at nine Italian psychiatric outpatient services. Assessments at T0 and T1 included the Generalized Anxiety Disorder 7-Item (GAD-7) for anxiety symptoms, and the Patient Health Questionnaire-9 (PHQ-9) for depressive symptoms. Differences in anxiety and depressive symptoms rates emerged across different mental disorders and a general improvement at T1 was detected for all of them in both the GAD-7 and PHQ-9 scores, except for Psychosis and Obsessive-Compulsive Disorder (OCD). Patients with Feeding and Eating Disorders (FED) reported statistically significantly higher: GAD-7 scores than those with Bipolar Disorder (BD), at both times, and Anxiety Disorders at baseline; PHQ-9 scores than all other diagnostic categories, at both times. Unemployment, no COVID-19 infection, OCD were predictive variables related to GAD-7 scores at T1, while being unmarried, BD or FED related to PHQ-9 scores at T1. Subjects with mental disorders reported anxiety and depressive symptoms during the third pandemic wave and most of patients showed an improvement over a 3-month follow-up, despite differences emerged among diagnostic categories and for the variables involved. Further studies are needed to deepen knowledge on pandemic impact on patients with mental disorders.

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1. Introduction

The COVID-19 pandemic has represented one of the most challenging global health emergencies of last three years due to the huge medical impact and the social and economic consequences (Nicola et al., 2020). The lockdown and restrictions due to the pandemic have generated a high alert and stressful state among the general population. Specifically, an increase in mental disorders, including the onset of mood and anxiety symptoms, has been reported in individuals with no prior mental disorder (Wang et al., 2020; Solomonov et al., 2022; Kestel et al., 2022). Likewise, the pandemic has proved to be a risk factor for those who already suffered from a mental disorder exacerbating states of anxiety, stress and depression (Plunkett et al., 2021; Hassan et al., 2022).

A worsening in psychiatric symptoms, with high levels of anxiety, depressive and post-traumatic stress symptoms have been reported in individuals with mood disorders associated with the lockdown (Carmassi et al., 2022; Zhang et al., 2021). Loneliness and boredom have been reported as risk factors of anxiety and depression in patients with preexisting depressive episodes (Oliè et al., 2022), besides being linked to problematic Internet use (Orsolini et al., 2023). In the early phase of the pandemic, a greater reduction in mental well-being was observed in patients with prior psychotic disorders than in those with mood disorders, especially for psychotic symptoms (Barrett et al., 2022). Overall, increased psychological distress appeared to be associated with poor social support and loneliness in both patients with prior severe mood and psychotic disorders (Pinkham et al., 2020). Most studies reported a general worsening of symptoms in individuals with pre-existing Obsessive-Compulsive Disorder (OCD) (Linde et al., 2022), during the initial phase of the pandemic, despite rates of individuals with a clinically significant worsening of symptoms ranged widely, from 36% (Benatti et al., 2020) to 76% (Van Ameringen et al., 2022). Predictors of worsening OCD included being younger, having comorbid General Anxiety Disorders (GAD) or Major Depressive Disorder (MDD) and having high contamination symptoms (Benatti et al., 2020). A 37% of individuals with OCD showed a clinically significant worsening of OC symptoms during the second wave of the pandemic in Italy, confirming the impact on OCD symptoms of the lockdown and/or restrictive measures associated with pandemic waves (Benatti et al., 2022). Some patients with OCD felt better during the waves of the pandemics, when lockdown measures were adopted and individuals had to be confined at home, while suffered from a worsening of symptoms when quarantine measures had been lifted and they were supposed to face again the world outside their homes (Jelinek et al., 2021; Fineberg et al., 2021). For what concerns subjects with Feeding and Eating Disorders (FEDs), increased number of hospitalizations, changes in body mass index and specific psychopathology (e.g. binge eating and purging behaviors), with timing specific changes related to lockdown measures (Devoe et al., 2022), besides an increase of anxiety and depressive symptoms (Khraisat et al., 2022), have been reported.

Although cross-sectional data on anxiety and depressive symptoms are available in people with various mental disorders, no study has evaluated their trend over time and across the subsequent pandemic waves. The COVID-19 pandemic, in fact, has been associated to unfavorable mental health outcomes, not only because of the impact of the contagion threat, with concerns about individuals' own health and the health of their loved ones, but also because of the lockdown measures adopted, affecting daily lives (Tzur Bitan et al., 2022; Fiorillo et al., 2020; Fiorillo and Gorwood, 2020; Wang et al., 2022). Further, the repeated easing of the restrictive measures upon the drop in the number of infections, and their subsequent tightening as the virus threat increased, may also have contributed to an additional traumatic burden. So far, however, little data has been reported on the longitudinal impact of the pandemic, particularly on people with a preexisting mental disorder (Benke et al., 2022; Fiorenzato and Cona, 2022; Coleman et al., 2022). To fill this gap, the aim of the present study was the prospective

assess anxiety and depressive symptoms in a sample of patients with different mental disorders naturalistically followed in different university psychiatry units across Italy during the COVID-19 pandemic and across subsequent waves of the infection. For this purpose, the sample was enrolled one year after the beginning of the pandemic, during the so-called third Italian wave of infection, during strict national containment measures and reassessed three months later, during a regression of the spread virus. Aim of the present study was also to explore the possible impact of socio-demographic variables, as well as of COVID-19 pandemic related variables affecting subjects, to these symptoms. Our hypothesis was that anxiety and depressive symptoms differed across different mental disorders and over time, showing an improvement along time with the easing of lockdown and social distancing measures adopted by the government to contain the pandemic. We also hypothesized a major role of socio-demographic and COVID related variables on these changings.

2. Methods

2.1. Study sample

This is a multicenter, naturalistic, 3-month longitudinal study, on a sample of 527 subjects with different mental disorders consecutively enrolled at the psychiatric outpatient services of nine Italian university clinics (Pisa, Bologna, Catania, Florence, Naples, Rome, Trieste, Turin, Verona). Enrollment (T0) started one-year after the COVID-19 pandemic onset, between March 15th to April 15th, 2021, during the third wave of the COVID-19 pandemic, while strict containment measures were in place in Italy. Patients were assessed again between 15th June to 15th July 2021 (T1; after 3 months from T0), during a phase of epidemiological regression of the viral spread, with consequent easing of measures and return to living conditions resembling the usual ones.

During the enrollment phase, all patients, aged 18 years or older, seeking a first or follow-up psychiatric visit were asked to participate and were diagnosed by Structured Clinical Interview for the Disorders of the DSM-5 (First et al., 2016) by skilled psychiatrists. Exclusion criteria were as follows: lack of knowledge of the Italian language or other limitation in verbal communication that impair the subject's ability to follow the protocol of assessment, intellectual disability and diagnosis of neurocognitive disorder according to DSM-5 criteria.

Drop-out rate between the two time-assessments was 17.84% ($N = 94$). Furthermore, 2 subjects were excluded because of missing data. Hence, the final sample for the present study encompassed 431 subjects.

A written informed consent was obtained to all participants after receiving an accurate description of the study. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Coordinating center (Pisa), Area Vasta Nord-Ovest Toscana (Italy), and of each participating center.

2.2. Instruments and assessments

All participants were asked to complete at baseline (T0) the Generalized Anxiety Disorder 7-Item (GAD-7) for anxiety symptoms (Spitzer et al., 2006) and the Patient Health Questionnaire-9 for depressive symptoms (Spitzer et al., 1999). At T1 the GAD-7 and PHQ-9 were administered again. According to previous studies (Carmassi et al., 2020, 2022), sociodemographic and clinical data were registered with a specific datasheet reporting information on the COVID-19 pandemic at baseline.

Socio-demographic (age, gender, marital status, housing status, education level, employment status), clinical data (previous psychiatric diagnoses and psychopharmacological treatments, medical comorbidity) and a set of information on the pandemic scenario (particularly 10 questions about COVID-19 pandemic, e.g. family members at risk for COVID-19 complications, COVID-19 infection of the probands or of close ones, etc.) were collected in a specific datasheet at baseline (T0).

Table 1Socio-demographic characteristics and related GAD-7 and PHQ-9 total scores at T0 and T1 in the total sample ($n = 431$).

Socio-demographic characteristic	N (%)	GAD-7 T0 mean (SD)	GAD-7 T1 mean (SD)	PHQ-9 T0 mean (SD)	PHQ-9 T1 mean (SD)
Age					
<42 years	212 (49.2%)	10.95 (5.72)	9.40 (5.68)	13.19 (6.98)	10.80 (6.80)
≥ 42 years	219 (50.8%)	10.13 (6.31)	8.11 (6.01)	11.53 (7.05)	8.31 (6.38)
p		.160	.023	.015	<0.001
Gender					
Female	267 (61.9%)	11.28 (5.83)	9.15 (5.94)	13.13 (6.89)	10.03 (6.76)
Male	164 (38.1%)	9.32 (6.17)	8.08 (5.74)	11.07 (7.15)	8.72 (6.54)
p		.001	.066	.003	.046
Civil status					
Unmarried/divorced	272 (60.8)	11.07 (6.00)	9.39 (5.92)	13.09 (6.96)	10.61 (6.75)
Married/cohabiting	159 (36.9)	9.62 (6.00)	7.64 (5.65)	11.08 (7.06)	7.69 (6.21)
p		.016	.003	.002	<0.001
Parental status					
Children (no)	262 (60.8)	10.52 (5.95)	9.04 (5.83)	12.75 (6.97)	10.25 (6.77)
Children (yes)	162 (39.2)	10.56 (6.17)	8.28 (5.94)	11.73 (7.16)	8.43 (6.46)
p		.937	.194	.143	.006
Education level					
High school degree (no)	113 (26.2)	11.50 (6.20)	9.04 (6.45)	13.09 (7.33)	9.51 (7.10)
high school degree (yes)	318 (73.8)	10.19 (5.94)	8.64 (5.67)	12.08 (6.94)	9.54 (6.57)
p		.046	.563	.194	.970
Employment					
Unemployed	232 (53.8)	11.30 (5.93)	9.83 (5.96)	13.29 (7.06)	10.74 (6.94)
Employed	199 (46.2)	9.64 (6.04)	7.48 (5.54)	11.25 (6.90)	8.13 (6.14)
p		.004	<001	.003	<0.001
Living condition					
a. Living alone	99 (23.0)	10.72 (6.10)	8.56 (5.70)	12.97 (6.44)	9.86 (6.56)
b. Living with family	194 (45.0)	9.83 (6.03)	8.12 (5.87)	11.22 (6.90)	8.39 (6.42)
c. Living with parental family	138 (32.0)	11.25 (6.20)	9.64 (5.92)	13.49 (7.48)	10.91 (6.94)
p		.067	.063	.009	.003
Post-hoc analysis					
Psychiatric history		–	–	$b < c$	$b < c$
First examination	126 (29.2)	10.06 (5.98)	7.75 (5.85)	12.35 (7.24)	9.41 (7.03)
Follow-up	30 (70.8)	10.73 (6.05)	9.15 (5.85)	12.35 (6.97)	9.58 (6.57)
p		.291	.024	.998	.810

The GAD-7 is a self-assessment questionnaire used as a tool for screening and measuring the severity of anxious symptoms (Spitzer et al., 2006). Particularly, it investigates the frequency of anxious symptoms in the last two weeks using 7 items with a score ranging from 0 (never) to 3 (almost every day). GAD-7 has an excellent internal consistency (Cronbach's $\alpha = 0.92$), as well as test-retest reliability ($r = 0.83$). Scores over 10 suggest the presence of moderate to severe anxiety symptoms.

The PHQ-9 represents one of the most used self-assessment tools for the screening of depressive symptoms (Spitzer et al., 1999). It consists of 9 items that investigate the presence of depressive symptoms in the last two weeks, each evaluated on a scale from 0 (never) to 3 (almost every day). Scores over 10 have been shown to have a sensitivity of 88% and a specificity of 88% specificity for major depression. The test has good both internal consistency (Cronbach's $\alpha = 0.89$), and test-retest reliability ($r = 0.84$).

2.3. Statistical analyses

All statistical analyses were performed using the Statistical Package for Social Science, version 26.0 (SPSS Inc.). Quantitative variables were reported as mean \pm standard deviation (SD), whereas categorical variables were reported as percentages. All tests were two-tailed and a p value <0.05 was considered statistically significant.

Independent Student *t*-test was utilized to compare GAD and PHQ-9 total scores at T0 and T1 between socio-demographic and COVID-19 related dichotomous variables. Similarly, one-way ANOVA was calculated to compare GAD-7 and PHQ-9 total score at T0 and T1 among living conditions and diagnostic groups. Bonferroni test was computed for post-hoc analyses. Paired Student *t*-test was computed to compare GAD-7 and PHQ-9 total score at T0 and T1 within each diagnostic group and in the total sample.

A linear regression analysis was computed for each sociodemographic variable, COVID-19 related and diagnostic variables as independent variable, and the GAD-7 total score at T1 as a dependent variable, to evaluate the possible predictors of GAD-7 total scores at T1. Linear regression analyses were adjusted for GAD-7 total scores at T0. Furthermore, a linear regression analysis was computed for each socio-demographic, COVID-19 related and diagnostic variables as independent variable, and the PHQ-9 total score at T1 as a dependent variable, to evaluate the possible predictors of PHQ-9 total scores at T1. These linear regression analyses were adjusted for PHQ-9 total score at T0. Finally, two multiple linear regression analyses were computed to examine the strongest predictors of the GAD-7 and PHQ-9 total scores at T1 (dependent variables) respectively. Variables to be included as independent in the regression analyses were selected among those that resulted to be statistically relevant at the univariate linear regression analyses, corrected to GAD-7 or PHQ-9 at T0 total scores.

3. Results

3.1. Socio-demographic and clinical characteristics at T0 and T1

Out of 431 subjects assessed, 267 (61.9%) were females and 164 (38.1%) males. The mean age of the sample was 42.22 ± 16.67 years, and 219 subjects (50.8%) presented an age over 42 years (median of the sample). Subjects were diagnosed as follows: 29 (6.7%) Psychosis Spectrum Disorders (PSD); 86 (20.0%) Bipolar Disorder (BD); 148 (34.3%) Major Depressive Disorder (MDD); 45 (10.4%) Anxiety Disorder (AD); 22 (5.1%) Obsessive Compulsive Disorder (OCD); 55 (12.8%) Feeding and Eating Disorder (FED); 46 (10.7%) other disorders. For what concern socio-demographic characteristics, most patients were females (267, 61.9%), unmarried/divorced (272, 60.8%), without children (262, 60.8%) and with high school degree (318, 73.8%)

Table 2

COVID-19 related variables and their comparison on GAD-7 and PHQ-9 total scores at T0 and T1 in the total sample (n = 431).

	N (%)	GAD-7 T0 mean (SD)	GAD-7 T1 mean (SD)	PHQ-9 T0 mean (SD)	PHQ-9 T1 mean (SD)
Work difficulties due to COVID-19					
Yes	148 (34.3)	10.69 (5.76)	8.66 (5.88)	13.34 (7.24)	9.82 (6.85)
No	283 (65.7)	10.45 (6.17)	8.78 (5.89)	11.83 (6.91)	9.39 (6.63)
p		.699	.838	.035	.525
Economic Loss due to COVID-19					
Yes	101 (23.4)	11.26 (6.03)	9.32 (6.18)	13.42 (7.27)	10.35 (7.03)
No	330 (76.6)	10.31 (6.02)	8.57 (5.78)	12.02 (6.96)	9.28 (6.59)
p		.168	.262	.082	.164
Quarantine					
Yes	92 (21.3)	10.15 (5.63)	7.75 (5.84)	13.18 (7.06)	8.46 (6.54)
No	339 (78.7)	10.64 (6.14)	9.01 (5.87)	12.12 (7.05)	9.83 (6.72)
p		.495	.068	.200	.082
COVID-19 infection					
Yes	41 (9.5)	10.07 (6.04)	5.88 (4.76)	11.85 (7.34)	6.66 (5.23)
No	390 (90.5)	10.58 (6.04)	9.04 (5.91)	12.40 (7.03)	9.84 (6.77)
p		.610	<0.001	.638	.001
Relatives or Friends infected with COVID-19					
Yes	186 (43.2)	10.81 (5.88)	9.00 (5.95)	13.02 (7.25)	9.99 (6.99)
No	245 (56.8)	10.33 (6.15)	8.55 (5.83)	11.84 (6.87)	9.19 (6.47)
p		.414	.429	.084	.219
Bereavement due to COVID-19					
Yes	33 (7.7)	11.33 (5.81)	8.97 (6.02)	14.73 (6.94)	9.97 (6.91)
No	398 (92.3)	10.47 (6.05)	8.72 (5.88)	12.15 (7.04)	9.50 (6.69)
p		.429	.818	.044	.698

Table 3

GAD-7 and PHQ-9 total scores across diagnostic groups and between T0 and T1 at T0 and T1.

Diagnosis (N,%)	GAD-7 T0 mean (SD)	GAD-7 T1 mean (SD)	P	PHQ-9 T0 mean (SD)	PHQ-9 T1 mean (SD)	p
Total sample (433, 100)	10.53 (6.03)	8.74 (5.88)	<0.001	12.35 (7.06)	9.53 (6.70)	<0.001
a. PSD (29, 6.7)	9.28 (6.29)	7.38 (7.30)	.091	10.76 (6.66)	8.70 (7.18)	.078
b. BD (86, 20.0)	8.78 (6.30)	7.01 (4.85)	.007	11.77 (7.48)	7.61 (6.12)	<0.001
c. MDD (148, 34.3)	11.15 (5.59)	8.78 (5.93)	<0.001	12.54 (6.77)	9.14 (6.24)	<0.001
d. AD (45, 10.4)	8.96 (5.96)	7.69 (6.13)	.025	9.38 (6.27)	7.47 (6.64)	.036
e. OCD (22, 5.1)	9.82 (6.26)	10.91 (5.61)	.291	10.14 (7.30)	10.91 (6.93)	.445
f. FED (55, 12.8)	13.11 (5.59)	11.15 (5.75)	.010	16.25 (6.13)	13.53 (6.88)	.002
g. OD (46, 10.7)	11.43 (5.95)	9.83 (5.31)	0.74	13.11 (7.17)	11.33 (6.44)	.072
p	<0.001	<0.001		<0.001	<0.001	
Bonferroni Post-hoc test	f> b.d.	f> b.		f> a.b.c.d.e.	f> a.b.c.d. g>b.	

Caption: PSD: Psychosis Spectrum Disorders; BD: Bipolar Disorder; MDD: Major Depressive Disorder; AD: Anxiety Disorders; OCD: Obsessive Compulsive Disorder; FED: Feeding and Eating Disorder; OD: Other Diagnosis.

(Table 1). More than thirty percent (34.3%) of participants reported to have had work difficulties (e.g., periods of absence from work/work loss), 23.4% economic losses because of the pandemic, and one fifth (21.3%) had been quarantined; besides almost ten percent (9.5%) had contracted COVID-19 (Table 2).

For what concern the GAD-7 and PHQ-9 total scores, a statistically significant decrease emerged on both scales between T0 and T1: from 10.53 ± 6.03 to 8.74 ± 5.88 ($p < .001$) for the GAD-7 scores, and from 12.35 ± 7.06 to 9.53 ± 6.70 ($p < .001$) for the PHQ-9 scores (Table 3).

3.2. GAD-7 and PHQ-9 scores changes between T0 and T1 upon sociodemographic variables

Statistically significantly higher GAD-7 scores emerged at both T0 and T1 among unmarried/divorced with respect to married/cohabiting subjects (T0, 11.07 ± 6.00 vs 9.62 ± 6.00 , respectively, $p = .016$; T1, 9.39 ± 5.92 vs 7.64 ± 5.65 , respectively, $p = 0.003$) and unemployed with respect to employed subjects (T0, 11.30 ± 5.93 vs 9.64 ± 6.04 , respectively, $p = .004$; T1, 9.83 ± 5.96 vs 7.48 ± 5.54 , respectively, $p < .001$) (Table 1).

Statistically significantly higher GAD-7 scores emerged at T0 only among females compared to males (11.28 ± 5.83 vs 9.32 ± 6.17 , respectively, $p = .001$) and subjects without, compared to those with, high school degree (11.50 ± 6.20 vs 10.19 ± 5.94 , respectively, $p =$

.46).

Statistically significantly higher GAD-7 scores at T1 only emerged among subjects younger, compared to those older, than 42 years (9.40 ± 5.68 vs 8.11 ± 6.01 , respectively, $p = .023$) and subjects at follow-up visit compared to those at first examination (9.15 ± 5.85 vs 7.75 ± 5.85 , respectively, $p = .024$). For what concern the COVID-19 related variables, statistically significantly higher GAD-7 scores emerged in those who had not, compared to those who had, contracted the virus (9.04 ± 5.91 vs 5.88 ± 4.76 , respectively, $p < .001$) (Table 2).

Statistically significantly higher PHQ-9 scores emerged at both T0 and T1 among: subjects younger compared to those older than 42 years (T0, 13.19 ± 6.98 vs 11.53 ± 7.05 , $p = .015$; T1 10.80 ± 6.80 vs 8.31 ± 6.38 , $p = <0.001$); females compared to males (T0, 13.13 ± 6.89 vs 11.07 ± 7.15 , $p = .003$; T1 10.03 ± 6.76 vs 8.72 ± 6.54 , $p = .046$); unmarried/divorced compared to married/cohabiting subjects (T0, 13.09 ± 6.96 vs 11.08 ± 7.06 , $p = .002$; T1, 10.61 ± 6.75 vs 7.69 ± 6.21 , $p < .001$); unemployed compared to employed subjects (T0, 13.29 ± 7.06 vs 11.25 ± 6.90 , $p = .003$; T1, 10.74 ± 6.94 vs 8.13 ± 6.14 , $p < .001$); subjects living with parental family compared to those living with family (T0, 13.49 ± 7.48 vs 11.22 ± 6.90 , post-hoc test $p = .009$; T1 10.91 ± 6.94 vs 8.39 ± 6.42 vs, post-hoc test $p = .003$) (Table 1).

Statistically significantly higher PHQ-9 scores at T0 only were observed among subjects with work difficulties due to COVID-19 compared to those without (13.34 ± 7.24 vs 11.83 ± 6.91 , $p = .035$)

and in subjects who experienced compared to those who did not experience a significant loss due to the COVID-19 (T0, 14.73 ± 6.94 vs 12.15 ± 7.04, $p = .044$) (Table 2).

Statistically significantly higher PHQ-9 scores at T1 only, emerged among subjects without compared to those with children (10.25 ± 6.77 vs 8.43 ± 6.46, $p = .006$) and in those who had not compared to those who had contracted the COVID-19 infection (9.84 ± 6.77 vs 6.66 ± 5.23, respectively, $p = 0.001$) (Tables 1 and 2).

3.3. GAD-7 and PHQ-9 scores change between T0 and T1 across diagnostic groups

A statistically significant decrease in the GAD-7 scores between T0 and T1 emerged in subjects with a diagnosis of BD ($p = .007$), MDD ($p < .001$), AD ($p = .025$) and FED ($p = .010$). Comparing diagnostic groups, patients with FED showed higher scores than all other diagnostic groups, reaching statistically significance for BD at both T0 and T1 and for AD at T0 only (Table 3).

Similarly, the PHQ-9 mean total scores showed a statistically significant reduction between T0 and T1 in patients with a diagnosis of BD ($p < .001$), MDD ($p < .001$), AD ($p = .036$), and FED ($p = .002$). When comparing diagnostic groups, patients with a diagnosis of FED showed statistically significantly higher PHQ-9 scores than all other diagnostic groups ($p < .001$), except OD, at T0 and statistically significantly higher scores than all other diagnostic groups ($p < .001$), except OCD and OD, at T1. Further, at T1, patients with a diagnosis of OD reported statistically significantly ($p < .001$) higher scores than those with BD.

3.4. Predictors of GAD-7 and PHQ-9 scores

To investigate possible predictors of GAD-7 and PHQ-9 total scores at T1 among sociodemographic, COVID-19 related and diagnostic variables, we calculated linear regression analyses, corrected with GAD-7 or PHQ-9 total scores at T0 respectively. Variables associated to GAD-7 total score at T1 were: civil status (single) [$b = 1.059$ (SE = 0.508), $B = 0.087$, $p = 0.038$, CI 95% = 0.057 – 2.055]; unemployment [$b = 1.559$ (SE = 0.490), $B = 0.132$, $p = 0.002$, CI 95% = 0.595 – 2.522]; psychiatric history (follow-up) [$b = 1.077$ (SE = 0.537), $B = 0.083$, $p = 0.045$, CI 95% = 0.023 – 2.132]; no COVID-19 infection [$b = 2.916$ (SE = 0.823), $B = 0.146$, $p = < 0.001$, CI 95% = 1.299 – 4.534]; and OCD diagnosis [$b = 2.657$ (SE = 1.106), $B = 0.100$, $p = 0.017$, CI 95% = 0.484 – 4.830]. Furthermore, a multiple regression model was performed to evaluate the variables associated with the total GAD-7 score at T1 (Table 4) and results showed the following: being unemployed [$b = 1.417$, (SE = 0.498), $p = .005$, CI95% = 0.437 – 2.397]; no COVID-19 infection [$b = 0.662$, (SE = 0.811), $p = .001$, CI 95% = 1.069 – 4.256]; OCD diagnosis [$b = 2.617$, (SE = 1.084), $p = .016$, CI 95% = 0.486 – 4.747].

Variables associated to PHQ-9 total score at T1 were: age over 42 years [$b = -1.750$ (SE = 0.562), $B = -0.131$, $p = 0.002$, CI 95% = -2.854 – -0.645]; civil status (single) [$b = 2.022$ (SE = 0.582), $B = 0.146$, $p = 0.001$, CI 95% = 0.878 – 3.166]; parental status (children

yes) [$b = -1.354$ (SE = 0.575), $B = -0.099$, $p = 0.019$, CI 95% = -2.485 – -0.223]; unemployment [$b = 1.693$ (SE = 0.566), $B = 0.126$, $p = 0.003$, CI 95% = 0.580 – 2.805]; Living with parental family [$b = 1.255$ (SE = 0.605), $B = 0.087$, $p = 0.039$, CI 95% = 0.065 – 2.444]; Quarantine (no) [$b = 1.872$ (SE = 0.684), $B = 0.115$, $p = 0.006$, CI 95% = 0.528 – 3.216]; no COVID-19 infection [$b = 2.924$ (SE = 0.951), $B = 0.128$, $p = 0.002$, CI 95% = 1.055 – 4.794]; BD diagnosis [$b = -1.959$ (SE = 0.700), $B = -0.117$, $p = 0.005$, CI 95% = -3.335 – -0.583]; OCD diagnosis [$b = 2.548$ (SE = 1.279), $B = 0.084$, $p = 0.047$, CI 95% = 0.035 – 5.062] and FED diagnosis [$b = 2.610$ (SE = 0.856), $B = 0.130$, $p = 0.002$, CI 95% = 0.928 – 4.291]. Further, a multiple linear regression model was performed to evaluate which of these variables were most associated with the total PHQ-9 score at T1 (Table 5). The results showed that the associated variables were the following: civil status (single) [$b = 1.607$ (SE = 0.703) $p = .023$, CI 95% = 0.225 – 2.989]; BD diagnosis [$b = -1.432$ (SE = 0.697) $p = .040$, CI 95% = -2.802 – -0.063]; FED diagnosis [$b = 1.977$ (SE = 0.902), $p = .029$ CI 95% = 0.204 – 3.751].

4. Discussion

To the best of our knowledge, this is the first longitudinal study aimed at examining anxiety and depressive symptoms in a large sample of patients with different mental disorders assessed one year after the pandemic onset, at the time of the third COVID-19 pandemic wave in Italy, besides their longitudinal trajectories after three months, at the time of the easing of the restrictive social distancing measures and lockdowns, for the reduction of the viral spread. Anxiety and depressive symptoms emerged across different mental disorders with different rates at all time points. Statistically significantly higher mean scores mostly emerged in unmarried, unemployed, younger, female subjects, living with parental family and with no children, at both times. A general statistically significant improvement was detected at T1 for all diagnostic categories in both the GAD-7 and PHQ-9 scores, except for patients with PSD and OCD. Patients with FED reported statistically significantly higher GAD-7 scores than those with BD, at both times, and AD at baseline, besides statistically significant higher PHQ-9 scores than all other diagnostic categories at both times. Variables predictive of GAD-7 scores at T1 resulted to be unemployment, no COVID-19 infection and a diagnosis of OCD, while variables predictive of PHQ-9 scores at T1 were being unmarried and a diagnosis of BD or FED.

One of our main findings was the presence of anxiety and depressive moderate symptoms in patients with mental disorders, across all diagnostic groups at baseline, with a general improvement after three months, concomitantly with a phase of relevant regression of the virus spread and easing of restrictive social distancing measures. Our results on patients with mental disorders appear in line with data suggesting a global burden of anxiety and depression related to the COVID pandemic in the general population, especially in its early phases, with a significant decrease over time as pandemic restrictions eased (COVID-19 Mental Disorders Collaborators, 2021; Fancourt et al., 2021; Lok et al., 2023; Sampogna et al., 2021). Interestingly, results also highlighted

Table 4
Multiple linear regression: predictive variables related to GAD-7 total score at T1 in the total sample ($N = 431$).

	b (SE)	β	p	95.0% CI		Tolerance
				Lower bound	Upper bound	
K	-4.137 (1.830)	-	.022	-7.735	-0.540	-
GAD-7 T0 total score	0.468 (0.040)	0.480	<0.001	0.390	0.547	0.971
Civil status (single)	0.535 (0.513)	0.044	.297	-0.472	1.543	0.916
Unemployed	1.417 (0.498)	0.120	.005	0.437	2.397	0.908
Psychiatric history (follow-up)	0.962 (0.523)	0.075	.066	-0.065	1.990	0.992
COVID-19 infection (no)	0.662 (0.811)	0.133	.001	1.069	4.256	0.991
Obsessive Compulsive Disorder	2.617 (1.084)	0.098	.016	0.486	4.747	0.985

$R^2 = 0.311$; adjusted $R^2 = 0.301$.

Table 5Multiple linear regression: predictive variables related to PHQ-9 total score at T1 in the total sample ($N = 431$).

	b (SE)	β	p	95.0% CI		Tolerance
				Lower bound	Upper bound	
K	-2.503 (2.324)	-	.282	-7.071	2.065	-
PHQ-9 T0 total score	.434 (0.040)	0.458	<0.001	0.356	.512	0.933
Age (over 42 years)	-0.968 (0.705)	-0.072	.171	-2.354	.419	0.590
Civil status (single)	1.607 (0.703)	0.116	.023	0.225	2.989	0.636
Parental status (yes)	.527 (0.774)	0.038	.496	-0.994	2.048	0.513
Living condition (parental family)	-0.207 (0.726)	-0.014	.776	-1.635	1.221	0.640
Quarantene (no)	1.361 (0.749)	0.083	.070	-0.110	2.833	0.775
COVID-19 infection (no)	1.559 (1.052)	0.068	.139	-0.508	3.627	0.773
Bipolar Disorder	-1.432 (0.697)	-0.086	.040	-2.802	-0.063	0.940
Obsessive Compulsive Disorder	2.122 (1.261)	0.070	.093	-0.357	4.602	0.955
Feeding and Eating Disorder	1.977 (0.902)	0.098	.029	0.204	3.751	0.812

 $R^2=0.312$; adjusted $R^2=0.296$.

significantly higher symptoms among females, unmarried, unemployed subjects, living alone or with parental family and without children. Additionally, having experienced work difficulties and the loss of a loved one because of the pandemic was related to significantly higher depressive scores at baseline. Surprisingly, having experienced a COVID-19 infection appeared to be related to lower anxiety and depressive scores at follow-up. Female gender has been reported to represent a risk factor for the increasing of both anxious and depressive symptoms during the pandemic (Gobbi et al., 2020), however, some authors have highlighted how in pandemic circumstances females could report an opposite effect (Pinkham et al., 2020; Davidson et al., 2022). Similarly, the unmarried and unemployed status resulted to have a negative influence on both anxious and depressive symptoms (Pierce et al., 2021; Carmassi et al., 2020; Iob et al., 2020). This is in accordance with the evidence of the role of strong concerns about personal financial stability among patients with mental disorders (Shinn and Viron, 2020; Castellini et al., 2021; McIntyre et al., 2022; Stein et al., 2022) hence the provision of adequate support to people in precarious economic conditions (Shinn and Viron, 2020). A significant decrease in the percentages of employed people with severe mental disorders (Sánchez-Guarnido et al., 2021), such as schizophrenia and BD, has been highlighted during the COVID-19 pandemic, because of the high burden of disease and disability, leading to more physical health problems, higher rates of premature death, greater risk of loneliness and social isolation (Shinn and Viron, 2020). In this regard, patients with psychoses may report an additive negative effect of the pandemic, due to the high rates of work loss that occurred among subjects with already low pre-pandemic rates of work and social functioning (Bucci et al., 2018), addressing the fact that patients with psychoses did not significantly improve along time. Interestingly, a positive association was found between housing condition and depressive symptoms only. Specifically, subjects living with their parental family reported the worse scoring.

Interestingly, a decrease in depressive and anxiety symptoms along time occurred with a statistically significant difference among patients with BD, MDD, AD and FED, despite differences in mean scores across diagnostic groups emerged at both baseline and follow up with patients with FED always reporting the highest scores with respect to the other diagnostic groups, particularly for what concern depressive scores. Furthermore, patients with OCD showed substantially stable depressive symptoms, with only a slight increase at follow-up, besides a worsening in the anxiety scores. These data seem to support previous evidence suggesting significant levels of psychiatric symptoms among patients with FED and OCD during the COVID pandemic (Jelinek et al., 2021; Fineberg et al., 2021; Gobbi et al., 2020; Pinkham et al., 2020; Treasure et al., 2022). Despite the former group showed an improvement across time, with the easing of containment measures, the latter reported lower despite more stable scores across time. This in contrast with what reported in patients with mood disorders, BD and MDD that, despite reporting similar or even higher anxiety and, particularly, depressive

scores at baseline, showed a deeper decrease over time, suggesting higher sensitivity to the easing of the restrictive measures and global improvement in the pandemic. Patients suffering from AD also showed a well-being trend, in line with the literature (Zhou et al., 2020), with an improvement in symptoms of anxiety and depression at the time of easing of the restrictive measures. More specifically, when comparing diagnostic subgroups, we found the highest depressive rates at baseline among subjects with FED diagnosis, together with the lowest improvement at 3-month follow-up in depressive symptoms, maintaining the highest mean scores across diagnostic groups. According to Touyz et al. (2022) and Monteleone et al. (2021), patients with FED diagnosis appear to be particularly impaired from the restriction about their maladaptive habits. These data show how subjects suffering from FED could show a specific sensitivity to the restrictions due to the pandemic. This vulnerability could be partially explained with an average 48% increase in hospitalizations during the pandemic, compared to previous pre-pandemic period, as described by a recent review of Devoe et al. (2022), but also to the exacerbation of the maintaining factors due to the lockdown measures (e.g. increased drive for thinness, emotional eating, increased PTSD symptoms during the isolation). Finally, our results show the lowest improvement in both anxiety and depressive symptoms among subjects with a diagnosis of OCD. These data appear to be in line with previous works: even if there are only few research about this newly introduced topic, the majority of studies found a general worsening of OC symptoms (i.e. up to 76% of individuals with pre-existing OCD presented a significant worsening of symptoms (Van Ameringen et al., 2022) associated with the pandemics. However, a significant proportion of subjects with OCD experienced a relief in anxiety and OC symptoms during the lockdown or the quarantine, when they did not have to face the challenge of exposing them to the world outside their homes. Our data showing that individuals with OCD did not show a general improvement in anxiety and depressive symptoms with the ease of the quarantine are in line with recent studies showing that some individuals with OCD do have difficulties adjusting to the easing of COVID-19 lockdown restrictions (Fineberg et al., 2021). Therefore, we could claim how subjects with a diagnosis of OCD suffered chronically the impact of the COVID-19 pandemic, with a prolonged impairment also lasting during the easing of restrictive measure and social distancing.

When discussing our results, some strengths and limitations should be considered. The main strength is that this study represents one of the few longitudinal studies on a clinical sample of subject with different mental disorders assessed during the COVID-19 pandemic. Nevertheless, anxious and depressive symptoms were collected using self-report instruments, which could be considered less accurate than a clinician assessment, even if they are widely used tools and with good clinical validity. We may also highlight the fact that the number of patients we enrolled with psychosis, FED or OCD is high with respect to other diagnoses that are more prevalent in the general population. This may be

related to the fact that most of the clinics involved are University centers, with high level of specialization, and this may affect the data, however we argue the fact this was not an epidemiological study. Further, data about previous hospitalization of returning patients were not available, and this may have had an impact on results. Lastly, the lack of pre-pandemic data about anxious and depressive symptoms in the subjects enrolled in the study.

In conclusion, the present study shows that patients have high levels of anxiety and depression which tend to decrease over time. This is not true for those affected by with FED and OCD, who therefore represent two subsamples of more fragile subjects, to whom specific and targeted interventions should be dedicated.

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Ethical standards

Ethical standards: A written informed consent was obtained to all participants after receiving an accurate description of the study. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Coordinating center (Pisa) (ID:17152/2020), Area Vasta Nord-Ovest Toscana (Italy), and of each participating center.

CRedit authorship contribution statement

Claudia Carmassi: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing. **Sarah Tosato:** Investigation, Writing – review & editing. **Virginia Pedrinelli:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Carlo A. Bertelloni:** Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. **Giovanni Abbate-Daga:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Umberto Albert:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Giovanni Castellini:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Mario Luciano:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Marco Menchetti:** Investigation, Writing – review & editing. **Maurizio Pompili:** Investigation, Writing – review & editing. **Gaia Sampogna:** Investigation, Writing – review & editing. **Maria Signorelli:** Investigation, Writing – review & editing. **Gabriele Massimetti:** Formal analysis. **Andrea Fiorillo:** Investigation, Methodology, Writing – review & editing.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

Data availability

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy reasons given nature of the data.

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