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Trauma Shaping the Psychopathological Correlates of Patients with Long-COVID: A 6-Months Longitudinal Study with Repeated Measures Mixed Models

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ABSTRACT

This research aimed at investigating how the experience of trauma can influence the psychological correlates of long-COVID over time in a clinical sample of patients hospitalized because of COVID-19. Through a longitudinal research design, 70 post-acute patients with COVID-19 were followed-up after hospital discharge in 3-time points up to 6 months and completed the Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5) and the Symptoms Checklist-90-Revised (SCL-90 R). Repeated measures mixed models with random intercept were used to evaluate the effect of trauma (yes/no) over time (T1, T2, T3) on the SCL-90-R scales. Results showed that patients with trauma display significantly worse psychological outcomes in all the SCL-90-R dimensions [all $p_{adj} < .05$ for the principal effects of trauma(y)], especially in symptoms of depression [time 2 *vs* time 1*trauma(y): b = -3.86, 95% CI (-7.18, -0.53), $p_{adj} = .035$; time 3 *vs* time 1*trauma(y): b = -4.77, 95%CI (-8.10, -1.45), $p_{adj} = .011$], anxiety [time 3 *vs* time 1*trauma(y): b = -4.54, 95%CI (-7.72, -1.37), $p_{adj} = .011$], and obsessive-compulsive difficulties [time 3 *vs* time 1*trauma(y): b = -4.03, 95%CI (-7.20, -0.86), $p_{adj} = .027$]. These findings shed light on the long-term psychological consequences of COVID-19 among hospitalized patients and highlight the key role of trauma, suggesting its assessment to tailor psychological interventions.

Introduction

Scientific literature has placed growing emphasis on the importance of the psychological impact of physical illness, acknowledging and comprehending its role for individual health, both mental and physical (e.g., Leventhal, 2002; Ogden, 2005; Singer et al., 2011). Mental and physical health are intertwined in a complex interaction (Doherty & Gaughran, 2014). Indeed, the psychological experience associated with illness significantly contributes to general psychological well-being of the individual. Research has demonstrated that long-term complications of physical illnesses in any bodily system can significantly impact the mental health of individuals, who may become more vulnerable to developing psychiatric disorders (Abraham et al., 2016). Importantly, physical illness threatens and compromises individuals' lives to the extent that it can represent a traumatic event itself (Parker et al., 2015).

As illness can represent a traumatic experience, trauma itself has an important impact in shaping psychological issues, also in a vicious cycle (Agaibi & Wilson, 2005; Shahar et al., 2013). The detrimental impact of trauma on mental health and its association with various psychological issues is widely recognized, both during the traumatic experience itself and in the subsequent months and years (Friedman & Keane, 2007), also through other maintaining processes (e.g., emotion dysregulation) (Rossi, Panzeri, & Mannarini, 2022; Weis et al., 2022). A recent umbrella literature review (Hogg et al., 2023) showed that psychological trauma represents a transdiagnostic risk factor across psychiatric conditions; moreover, trauma is known to be associated with poorer

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physical health outcomes over time (for a review, see Pacella et al., 2013).

COVID-19 disease as a potential traumatic event

COVID-19 is a virus able to cause a disease with a potentially severe psychological impact. Although the World Health Organization (WHO) announced the end of the COVID-19 pandemic in May 2023, the global community continues to grapple with its enduring repercussions, encompassing social, economic, and psychological aspects (WHO, 2023).

Moreover, COVID-19 was revealed to be an issue also after its acute phase. Indeed, the so-called 'long-COVID illness' (Davis et al., 2023) includes the manifestation of COVID-related symptoms – both physical (e.g., cough, fatigue, breathlessness) and psychological (e.g., anxiety, depression) – even after the recovery from the acute phase (Zeng et al., 2023). After more than three years since the pandemic began, a concerning number of COVID-19 survivors is showing the various sequelae of COVID disease (He et al., 2023; Zürcher et al., 2022).

Importantly, the COVID-19 disease itself and its associated factors, including treatments and experiences such as isolation, have the potential to be traumatic (Rossi et al., 2022; Thakur & Jain, 2020; Zhang et al., 2021). Indeed, COVID-19 disease in its acute phase can be a life-threatening condition and can represent a trauma, especially for individuals with severe cases requiring hospitalization and additional treatments like intubation (Nagarajan et al., 2022). Particularly, most patients with severe COVID-19 have experienced potentially traumatic circumstances, including undergoing physically invasive medical procedures (e.g., tracheotomy), facing the risk of their own death, assisting someone else in a life-threatening or fatal situation – both at the hospital or at home – and possibly infecting relatives to the risk of death or already deceased (Rossi Ferrario et al., 2021).

Post-traumatic symptomatology and broader psychological impact of the COVID-19 disease

According to the literature, patients who have been hospitalized due to COVID-19 face a higher likelihood of experiencing intrusion and hyperarousal symptoms (Craparo et al., 2022). Also, a systematic literature review (Schou et al., 2021) reported that the post-traumatic stress disorder (PTSD) rate among COVID-19 patients after discharge is up to 42.8% (i.e., Bellan et al., 2021).

A review of studies from worldwide (Schou et al., 2021) showed that PTSD is widespread (up to 43%) among COVID-19 survivors after hospital discharge up to 7 months later. In the Italian context, a study showed that three months after discharge the prevalence of PTSD provisional diagnosis (measured with the Post-traumatic Stress Disorder Checklist; PCL-5, Weathers, et al., 2013) was around 10.4%, and a subthreshold diagnosis was about 8.6% (Tarsitani et al., 2021). Importantly, the literature showed that the severity of PTSD symptoms can predict the presence of prolonged psychological symptoms over time (Poyraz et al., 2021).

After three years of pandemic, it is well known that a potentially traumatic experience such as COVID-19 has a psychological impact not only limited to post-traumatic stress symptoms, but also broader and multifaceted. Indeed, a recently published review (Zeng et al., 2023) (with search up to Sep. 30th, 2021) found that after acute COVID-19 disease, the predominant psychiatric outcomes observed between 6 to 12 months were anxiety (15.4%, 95%CI [8.0,24.6]), depression (12.4%, 95%CI [5.8, 21.1]), and sleep disturbance (12.3%, 95%CI [4.8, 22.6]).

In patients with prolonged symptoms of COVID-19, COVID-19 is clearly an objective event, but trauma is a subjective psychological experience too: thus, it is crucial to assess the progression of related psychopathological characteristics – both the stable ones and the others that worsen or improve – because shedding light on these aspects could have important clinical implications in terms of psychological intervention.

The present study

At the same time, the current knowledge of the psychological implications of the long-COVID illness is fragmented and needs further investigation for different reasons.

The first reason is about the constructs. Indeed, most of the literature focused mainly on anxiety and depression, but did not consider the effect of other variables – e.g., traumatic symptoms – also in large observational longitudinal studies (e.g., Fancourt et al., 2023). This specific focus on anxiety and depression is probably because of the several evidence from the general population, which showed their well-established increase during the COVID-19 pandemic, spanning from children and adolescents (umbrella review, Hossain et al., 2022), adults (Hajek et al., 2022; Johnson et al., 2022; Rudenstine et al., 2022; Scarfe et al., 2023), to the elderly (a scoping review, Lau et al., 2023).

The second reason concerns the populations precisely. Despite more detailed evidence coming from the general population, evidence on clinical populations from treatment centers or hospitals is still rather limited (Bourmistrova et al., 2022). The third reason is related to the study design, as mental health trajectories over time are often overlooked. In fact, the number of updated longitudinal studies examining the multiple psychological correlates of long-COVID patients over the mid-long term (up to 6 months after discharge) is less than the cross-sectional studies (Bourmistrova et al., 2022).

Moreover, evidence from the Italian context – one of the first countries to experience the spread of the epidemic – is even more limited (Bruno et al., 2020).

Summarizing, all these reasons outline a rather incomplete scenario, the gaps of which are worth trying to fill. In this fast-expanding field, it is important to collect more updated studies to investigate the multifaceted psychological sequelae of COVID-19 in the mid-long term in relation to traumatic experiences, a critical component of life-threatening conditions. In summary, the scientific literature is currently working to establish more robust evidence regarding: *i)* the psychological correlates of long-COVID disease beyond anxiety and depression, *ii)* the longitudinal impact of psychological factors such as trauma, *iii)* in patients with long-COVID; and *iv)* within the Italian context.

Given this background, the present study aims to:

- explore the impact of trauma related to COVID-19 on psychological conditions, including but not limited to depression and anxiety, in a longitudinal fashion that extends up to 6 months after the first negative swab, in a sample of patients hospitalized for COVID-19;
- describe and compare the trajectories of patients with and without trauma related to COVID-19 over time.

According to the literature (for a review, Hogg et al., 2023), trauma was hypothesized to be associated with higher psychological symptoms and less favorable psychological outcomes over time, particularly in state-like characteristics – such as anxiety and depression - and to a lesser extent in trait-like characteristics. Due to the novelty of the topic with still relatively limited research evidence, it was not possible to formulate more specific hypotheses.

Methods

2.1. Study design

A longitudinal research design was used; the study flow diagram is in the Supplementary Materials. Participants were continuously screened for enrolment in the study during their hospitalization for COVID-19 disease from March 2020 to May 2021 at the Padua hospital, Italy.

Inclusion criteria for the present study were: *i)* being hospitalized with COVID-19 disease; *ii)* age over 18 years old; *iii)* fluently speaking

Italian; *iv)* completion of the assessment points up to 6 months after the first negative swab. Exclusion criteria were: *v)* the presence of inadequate conditions preventing from undergoing or completing the assessment (e.g., cognitive impairment, sensorial or motor deficits, contrary medical advice). An interview was conducted by a clinical psychologist specialized in psychotherapy to determine the eligibility of each patient for the study.

Participants completed the assessment at 3 time points: time 1) one month after the first negative swab; time 2) follow-up after 3 months from the first negative swab; time 3) follow-up after 6 months from the first negative swab. To note, in studies with consecutive enrolment as the present one, time is often a relative variable (taking an event as reference point) and not an absolute variable (e.g., Fancourt et al., 2023).

Follow-up assessments were planned after 3 and 6 months for theoretical and practical considerations (Galante et al., 2023; National Collaborating Centre for Mental Health, 2018). These time points offer a critical window to observe psychological adaptations following illness onset, capturing short- and short- to medium-term effects. The 3- and 6-month durations strike a balance between providing a sufficiently extended observation period and minimizing the impact of extraneous variables. This approach protects against uncontrollable intervening events and prevents significant sample loss. Additionally, these time frames coincide with routine medical check-ups, ensuring participant retention and aligning with existing clinical schedules for practical implementation. Furthermore, this timing is consistent with the common usage in the literature, facilitating meta-analyses and cross-study comparisons. This study was in accordance with the Declaration of Helsinki on Human Rights and was approved by the Ethics Committee of the Padova University Hospital (Prot. N. 0014424). All participants provided a written informed consent to participate. Data from this study are part of a larger research project (Devita et al., 2021, 2022).

Measures

A combination of clinical interviews and self-report tools was used for longitudinal psychological assessment.

Clinical interview

During patient enrollment and throughout the study time points (1, 2, 3), a clinical psychologist specialized in psychotherapy conducted individual clinical interviews with the (ex)patients to: *i)* verify that COVID-19 was the most traumatic event in the last months; *ii)* administer the self-report survey in paper and pencil, making sure that participants could take breaks if needed; *iii)* check the congruence between the interview and the results of the self-reports – to reduce their potential biases – and no discrepancy emerged.

Self-report survey

The whole survey took an average completion time of around 30-40 minutes and consisted of the following self-report assessment tools.

A *socio-demographic survey* containing questions about age, biological sex, education, and occupation. It was administered only at time 1.

The *Post-traumatic Stress Disorder Checklist* (PCL-5, Weathers, et al., 2013) is a self-report measure suitable for the screening of Post Traumatic Stress Disorder (PSTD). PCL-5 consists of 20 items describing the symptoms of PTSD symptoms according to the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5, American Psychiatric Association, 2013). Respondents rate how much each item has bothered them in the past month on a 5-point Likert type scale from 0 (= "not at all") to 4 (= "extremely") (e.g., "Avoiding memories, thoughts, or feelings related to the stressful experience?"). The total score is the sum of the items (range 0-80) and indicates the presence and severity of PTSD symptoms. A PCL-5 score above 31-33 indicates a provisional PTSD diagnosis. PCL-5 was administered only at time 1.

The *Symptoms Checklist-90-Revised* (SCL-90-R; Derogatis & Unger, 2010; Prunas et al., 2012) is a widely used self-report questionnaire to evaluate psychological and affective distress, providing a multidimensional symptom profile (Kostaras et al., 2020). SCL-90-R was administered at time 1, time 2, and time 3. Its items describe symptoms and are scored on a 5-point Likert-type scale from 0 (= not at all) to 4 (= extremely).

The combination of SCL-90-R items produces nine primary symptoms dimensions and three global indices. The primary symptom dimensions are Somatization (SOM), Obsessive-Compulsive (OC), Interpersonal Sensitivity (IS), Depression (DEP), Anxiety (ANX), Hostility and anger (HOS), Phobic Anxiety (PHOB), Paranoid Ideation (PAR), and Psychoticism (PSY) (Prinz et al., 2013). The 3 global indices (Prunas et al., 2012) are a linear transformation of the primary scales and capture the general psychological distress that is often associated with traumatic events (Zhang et al., 2021). They are: the Global Severity Index (GSI), which is the mean of all 90 items and combines information about the number of symptoms with the severity of perceived distress. It is considered the best indicator of the individual's distress intensity; the Positive Symptom Total (PST), reflecting the number of symptoms reported regardless of the level of distress and it is a measure of symptom breadth; the Positive Symptom Distress Index (PSDI), a measure of the intensity of symptoms, which is the average level of distress reported for the endorsed symptoms. It is the sum of all 90 items divided by the PST score.

For all the SCL-90-R 12 scales, the raw scores were transformed into T scores (mean = 50, SD = 10). The Italian version of the SCL-90-R showed good psychometric properties and good longitudinal sensitivity to change (Carrozzino et al., 2022; Prunas et al., 2012).

2.3. Statistical analysis

All analyses were performed with the R software version 4.2.2 (R Core Team, 2021) and R studio (RStudio Team, 2023), using the R packages *lme4* (Bates et al., 2023), *emmeans* (Lenth et al., 2022), *ggplot2* (Wickham, 2016). The α level was set at .05.

Preliminary Analyses

The preliminary analyses tested whether the final sample included in the analysis differed from the eligible individuals lost to follow-up or from the sample initially recruited. In the final sample, it was tested whether any medical variable influenced psychological outcomes. Descriptive statistics were then used on the final sample to describe its characteristics. All subjects (n = 70) included in the final analysis had complete observations at the three time points (n = 210).

Repeated Measures Mixed Models

Repeated measures mixed models were chosen because they are well suited for analyzing data with repeated measurements, as they offer robustness and flexibility (Detry & Ma, 2016). Indeed, mixed models are considered more flexible and less sensitive to various assumptions compared to repeated measures ANOVA (Armstrong, 2017); moreover, their robustness to violations of these assumptions has been proven (Loy et al., 2017; Schielzeth et al., 2020). These models are termed 'mixed' because they incorporate both fixed effects, which are the same for all observations (i.e., time, trauma, time*trauma), and random effects (i.e., subjects), which vary for each observation.

In this study, repeated measures linear mixed models were used to examine the influence of independent variables – time (3 levels: 1, 2, 3) and trauma (yes = 'trauma' group / no = 'no trauma' group) – on all the clinical scales of the SCL-90-R as separate dependent variables. Primary outcomes were the 9 primary scales of the SCL-90-R; secondary outcomes were the 3 global scales of the SCL-90-R (i.e., GSI, PSDI, PDT) because they are a linear transformation of the primary scales. An interaction term was included in the analysis between the trauma factor and time (time*trauma) to investigate how the recovery trajectories vary between different trauma groups. A random intercept was included

for each participant to explicitly account for the correlation over time between repeated measurements within each participant. Additionally, this random intercept helps to control for individual differences in the trajectory of outcomes experienced by each patient on their path toward reaching their outcome.

In this study, all assumptions of all mixed linear models were tested (i.e., outliers and influential cases with Cook's distance, independence of errors with the Durbin-Watson test, low multicollinearity with the variance inflation factor, normality of residuals and homogeneity of variance of residuals) and no violations emerged (Loy et al., 2017; Schielzeth et al., 2020).

In order to control the impact of biological sex, all models were run considered it as a covariate. However, it did not show statistically significant effects (all $p_{adj} > .05$) (see Supplementary Materials for more).

Multiple comparison correction

As the same statistical tests were conducted on multiple outcomes (the SCL-90-R scales), p-values were adjusted (p_{adj}) through a multiple comparison correction, the false discovery rate (Benjamini & Hochberg, 1995).

Results

Preliminary Analyses

The results of the preliminary analyses showed that the individuals in the final sample (n = 70) did not differ from those 'eligible but lost to follow-up' (n = 309) in terms of sociodemographic and medical variables (for more information, see the Supplementary Materials). Two small exceptions were that those included in the final sample showed slightly higher: education ($p = .080$, small-medium Cohen's $d = .24$); time from discharge to first assessment ($p = .202$, small Cohen's $d = .17$). Furthermore, preliminary analyses in the final sample showed that medical variables (e.g., disease severity, intubation, cognitive/neurological or physical symptoms) did not influence the psychological outcomes (all $p > .05$).

3.2. Descriptive statistics

The sample (N = 70) had an average age of 57.83 years (SD = 11.55, range = 26 – 85) and consisted mostly of females (59.7%). Table 1 shows the sociodemographic characteristics of the sample and some clinical information. The PCL-5 score at hospitalization (time 1) was used to split the sample into two groups: participants without a reported traumatic experience ('*no trauma*' group: PCL-5 < 31, $n = 35$, age: 59 ± 10.22, females 29%) and with a reported traumatic experience ('*trauma*' group: PCL-5 > 31, $n = 35$, age: 57 ± 12.83, female 54%). The two groups were homogeneous in terms of age and biological sex, showing non-statistically significant differences ($p > .05$) (respectively tested with t-test and chi-square test, with negligible to small effect-sizes – Cohen's d and φ).

Table 2 shows the scores of the SCL-90-R scales in the total sample across the trauma groups.

Table 1
Descriptive statistics of the sample characteristics

	Total (N = 70)		No-trauma ($n = 35$)		Trauma ($n = 35$)	
	n	%	n	%	n	%
Females	29	41%	10	29%	19	54 %
Males	41	59%	25	71%	16	46 %
	mean	sd	mean	sd	mean	sd
Age (years)	57.83	11.55	59	10.22	57	12.83
Years of education	13.34	4.85	14	5.02	13	4.74
PCL – time 1	32.43	13.40	21.69	4.33	43.17	10.40

Note: sd = standard deviation; PCL = Post-traumatic Stress Disorder Checklist.

Table 2
Descriptive statistics of the Symptoms-Check-List-90 Revised (SCL-90-R) scales in the total sample and across trauma groups.

		Total sample (N = 70)		No Trauma ($n = 35$)		Trauma ($n = 35$)	
variable	time	mean	sd	mean	sd	mean	sd
Primary Scales							
SOM	1	50.44	11.00	45.34	6.00	55.54	12.48
	2	50.04	18.02	44.63	7.50	55.46	23.29
	3	47.23	9.54	44.54	7.18	49.91	10.88
OC	1	49.84	13.89	42.83	6.50	56.86	15.75
	2	47.81	12.88	42.43	6.69	53.20	15.24
	3	46.77	11.79	41.77	5.44	51.77	14.19
IS	1	45.59	10.66	41.71	2.37	49.46	13.94
	2	45.94	11.88	41.89	2.52	50.00	15.70
	3	45.04	10.62	41.40	1.94	48.69	14.06
DEP	1	49.73	13.70	43.40	4.37	56.06	16.72
	2	48.37	13.51	43.97	6.37	52.77	17.03
	3	46.34	10.53	42.40	4.02	50.29	13.30
ANX	1	49.33	11.15	43.43	4.76	55.23	12.57
	2	48.96	13.05	43.63	6.51	54.29	15.65
	3	46.57	9.20	42.94	4.51	50.20	11.16
HOS	1	44.71	8.38	41.54	3.37	47.89	10.51
	2	45.44	9.72	41.91	3.33	48.97	12.45
	3	43.74	6.89	41.03	2.05	46.46	8.78
PHOB	1	55.29	17.67	49.77	8.46	60.80	22.35
	2	53.50	16.45	47.77	6.59	59.23	20.94
	3	50.50	12.35	45.91	3.02	55.09	16.03
PAR	1	43.64	8.89	40.46	2.63	46.83	11.52
	2	44.30	10.61	41.00	3.23	47.60	13.99
	3	43.76	10.52	40.40	2.78	47.11	13.92
PSY	1	48.33	12.70	43.89	3.04	52.77	16.66
	2	48.29	14.41	44.20	3.38	52.37	19.37
	3	47.50	12.17	42.49	0.98	52.51	15.74
Global scales							
GSI	1	48.14	12.98	41.80	4.26	54.49	15.53
	2	47.26	13.64	41.63	5.43	52.89	16.81
	3	45.49	11.58	40.66	3.89	50.31	14.45
PST	1	47.29	10.77	41.14	6.40	53.43	10.81
	2	46.89	11.91	41.09	7.06	52.69	12.99
	3	45.39	12.52	39.71	6.16	51.06	14.63
PSDI	1	48.17	10.79	43.46	6.43	52.89	12.22
	2	46.17	10.39	44.03	8.02	48.31	12.06
	3	43.37	9.97	40.80	9.57	45.94	9.82

Note: sd = standard deviation; SOM = Somatization; OC = Obsessive-Compulsive; IS = Interpersonal Sensitivity; DEP = Depression; ANX = Anxiety; HOS = Hostility; PHOB = Phobic Anxiety; PAR = Paranoid Ideation; PSY = Psychoticism; GSI = Global Severity Index; PST = Positive Symptom Distress Index; PST = Positive Symptom Total.

3.3. Repeated measures mixed models

Table 3 shows the results of the repeated measures mixed-effect models on the SCL-90-R scales (side by side), the upper part shows the fixed coefficients, and the lower part shows the random effects and information about the marginal and conditional R^2 – the first includes only the fixed effects, while the second accounts also for the random effects.

Fig. 1 shows the graphs of the predicted scores of the SCL-90-R scales over time (on the x-axis) and across the 'trauma' group with (in red, line above) and 'no trauma' group (in light blue, line below), the vertical bars show the 95% confidence intervals (CIs).

The results of the repeated measures mixed models (Table 3) show that living or not a traumatic experience (at time 1) had a statistically significant positive effect on all the SCL-90-R scales, both the primary ones (SOM: b = 10.2, CI [4.24, 16.16], $p_{adj} = .003$; OC: b = 14.03, CI [8.59, 19.46] $p_{adj} < .001$; IS: b = 7.74, CI [2.82, 12.66] $p_{adj} = .008$; DEP: b = 12.66, CI [7.14, 18.17] $p_{adj} < .001$; ANX: b = 11.8, CI [7.04, 16.56] $p_{adj} < .001$; HOS: b = 6.34, CI [2.65, 10.04] $p_{adj} = .003$; PHOB: b = 11.03, CI [4.04, 18.02] $p_{adj} < .007$; PAR: b = 6.37, CI [1.87, 10.87] $p_{adj} < .020$; PSY: b = 8.89, CI [3.04, 14.73], $p_{adj} < .011$) and the global scales

Table 3
Results of the mixed model on the Symptoms Check-List 90-Revised (SCL-90-R) scales: primary scales (3 parts) and global scales (part 4)

Primary outcomes: SCL-90-R Primary Scales - Part 1												
Fixed Part	**Somatization**				**Obsessive Compulsive**				**Interpersonal Sensitivity**			
Predictors	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}
(Intercept)	45.34	[41.13, 49.56]	<.001	<.001	42.83	[38.99, 46.67]	<.001	<.001	41.71	[38.23, 45.19]	<.001	<.001
time [2 *vs* 1]	-0.71	[-4.71, 3.28]	.725	.827	-0.4	[-2.64, 1.84]	.726	.726	0.17	[-1.53, 1.88]	.843	.843
time [3 *vs* 1]	-0.8	[-4.79, 3.19]	.693	.827	-1.06	[-3.30, 1.18]	.354	.425	-0.31	[-2.02, 1.39]	.717	.843
trauma (yes)	10.2	[4.24, 16.16]	.001	.003*	14.03	[8.59, 19.46]	<.001	<.001*	7.74	[2.82, 12.66]	.003	.008*
time [2 *vs* 1] × trauma (yes)	0.63	[-5.02, 6.27]	.827	.827	-3.26	[-6.43, -0.09]	.045	.067	0.37	[-2.04, 2.78]	.762	.843
time [3 *vs* 1] × trauma (yes)	-4.83	[-10.47, 0.82]	.094	.188	-4.03	[-7.20, -0.86]	.013	.027*	-0.46	[-2.87, 1.95]	.709	.843
Random Effects												
σ^2	71.7				22.62				13.09			
τ_{00}	88.33 id				110.35 id				95.94 id			
ICC	0.55				0.83				0.88			
R^2: Marginal / Conditional	0.126 / 0.608				0.214 / 0.866				0.122 / 0.895			

Primary outcomes: SCL-90-R primary scales - part 2												
Fixed part	**Depression**				**Anxiety**				**Hostility**			
Predictors	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}
(Intercept)	43.4	[39.50, 47.30]	<.001	<.001	43.43	[40.06, 46.80]	<.001	<.001	41.54	[38.93, 44.16]	<.001	<.001
time [2 *vs* 1]	0.57	[-1.78, 2.92]	.632	.632	0.2	[-2.04, 2.44]	.861	.861	0.37	[-1.68, 2.43]	.722	.722
time [3 *vs* 1]	-1	[-3.35, 1.35]	.403	.484	-0.49	[-2.73, 1.76]	.67	.804	-0.51	[-2.57, 1.54]	.622	.722
trauma (yes)	12.66	[7.14, 18.17]	<.001	<.001*	11.8	[7.04, 16.56]	<.001	<.001*	6.34	[2.65, 10.04]	.001	.003*
time [2 *vs* 1] × trauma (yes)	-3.86	[-7.18, -0.53]	.024	.035*	-1.14	[-4.32, 2.03]	.478	.718	0.71	[-2.19, 3.62]	.628	.722
time [3 *vs* 1] × trauma (yes)	-4.77	[-8.10, -1.45]	.005	.011*	-4.54	[-7.72, -1.37]	.005	.011*	-0.91	[-3.82, 1.99]	.536	.722
Random Effects												
σ^2	24.86				22.65				18.99			
τ_{00}	112.16 id				79.49 id				42.55 id			
ICC	0.82				0.78				0.69			
R^2: Marginal / Conditional	0.165 / 0.848				0.210 / 0.825				0.146 / 0.736			

Primary outcomes: SCL-90-R primary scales - part 3												
Fixed Part	**Phobic Anxiety**				**Paranoid Ideation**				**Psychoticism**			
Predictors	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}
(Intercept)	49.77	[44.83, 54.71]	<.001	<.001	40.46	[37.27, 43.64]	<.001	<.001	43.89	[39.75, 48.02]	<.001	<.001
time [2 *vs* 1]	-2	[-5.60, 1.60]	.275	.412	0.54	[-1.23, 2.32]	.547	.949	0.31	[-2.01, 2.64]	.790	.790
time [3 *vs* 1]	-3.86	[-7.45, -0.26]	.036	.073	-0.06	[-1.83, 1.72]	.949	.949	-1.4	[-3.72, 0.92]	.236	.474
trauma (yes)	11.03	[4.04, 18.02]	.002	.007*	6.37	[1.87, 10.87]	.006	.020*	8.89	[3.04, 14.73]	.003	.011*
time [2 *vs* 1] × trauma (yes)	0.43	[-4.66, 5.51]	.868	.868	0.23	[-2.28, 2.74]	.858	.949	-0.71	[-4.00, 2.57]	.669	.790
time [3 *vs* 1] × trauma (yes)	-1.86	[-6.94, 3.23]	.472	.567	0.34	[-2.16, 2.85]	.788	.949	1.14	[-2.14, 4.43]	.494	.741
Random Effects												
σ^2	58.21				14.15				24.3			
τ_{00}	161.66 id				77.06 id				129.41 id			
ICC	0.74				0.84				0.84			
R^2: Marginal / Conditional	0.128 / 0.769				0.107 / 0.861				0.119 / 0.861			

Secondary outcomes: SCL-90-R Global scales - Part 4												
Fixed Part	**GSI**				**PSDI**				**PST**			
Predictors	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}	est	95% CI	p	p_{adj}
(Intercept)	41.8	[37.96, 45.64]	<.001	<.001	43.46	[40.16, 46.76]	<.001	<.001	41.14	[37.73, 44.55]	<.001	<.001
time [2 *vs* 1]	-0.17	[-2.16, 1.82]	.865	.865	0.57	[-2.36, 3.50]	.701	.701	-0.06	[-2.24, 2.12]	.959	.959
time [3 *vs* 1]	-1.14	[-3.13, 0.85]	.259	.382	-2.66	[-5.59, 0.27]	.076	.091	-1.43	[-3.61, 0.75]	.197	.396
trauma (yes)	12.69	[7.26, 18.11]	<.001	<.001*	9.43	[4.76, 14.10]	<.001	<.001*	12.29	[7.46, 17.11]	<.001	<.001*
time [2 *vs* 1] × trauma (yes)	-1.43	[-4.24, 1.38]	.318	.382	-5.14	[-9.29, -1.00]	.016	.031*	-0.69	[-3.77, 2.40]	.661	.794
time [3 *vs* 1] × trauma (yes)	-3.03	[-5.84, -0.22]	.036	.071	-4.29	[-8.43, -0.14]	.043	.065	-0.94	[-4.02, 2.14]	.547	.794
Random Effects												
σ^2	17.81				38.66				21.36			
τ_{00}	114.76 id				59.41 id				83.39 id			
ICC	0.87				0.61				0.8			
R^2: Marginal / Conditional	0.200 / 0.892				0.133 / 0.658				0.252 / 0.848			

Note: GSI = Global Severity Index; PST = Positive Symptom Distress Index; PST = Positive Symptom Total. est = unstandirdezed estimate; 95%CI [lower, upper] = confidence interval; p = p value; p_{adj} = p adjusted for the false discovery rate; * = p < .05; σ^2 = random effect variance; τ_{00} = between-subject-variance; ICC = intraclass correlation coefficient; N subjects = 70; n observations = 210.

(GSI: b = 12.69, CI [7.26, 18.11] $p_{adj} < .001$; PSDI: b = 9.43, CI [4.76, 14.10] $p_{adj} < .001$; PST: b = 12.29, CI [7.46, 17.11], $p_{adj} < .001$). This means that reporting traumatic symptoms is associated with higher scores on all SCL-90-R scales.

Moreover, the interaction of trauma (yes) and time (trauma*time) was statistically significant for the following: DEP both when comparing time 2 *vs* time 1*trauma(y) (b = -3.86, CI [-7.18, -0.53], $p_{adj} = .035$) and when comparing time 3 *vs* time 1*trauma(y) (b = -4.77, CI [-8.10, -1.45], $p_{adj} = .011$); ANX only when comparing time 3 *vs* time 1*trauma (y) (b = -4.54, CI [-7.72, -1.37], $p_{adj} = .011$); OC only when comparing time 3 *vs* time 1*trauma(y) (b = -4.03, CI [-7.20, -0.86], $p_{adj} = .027$); and PSDI only when comparing time 2 *vs* time 1*trauma(y) (b = -5.14, CI

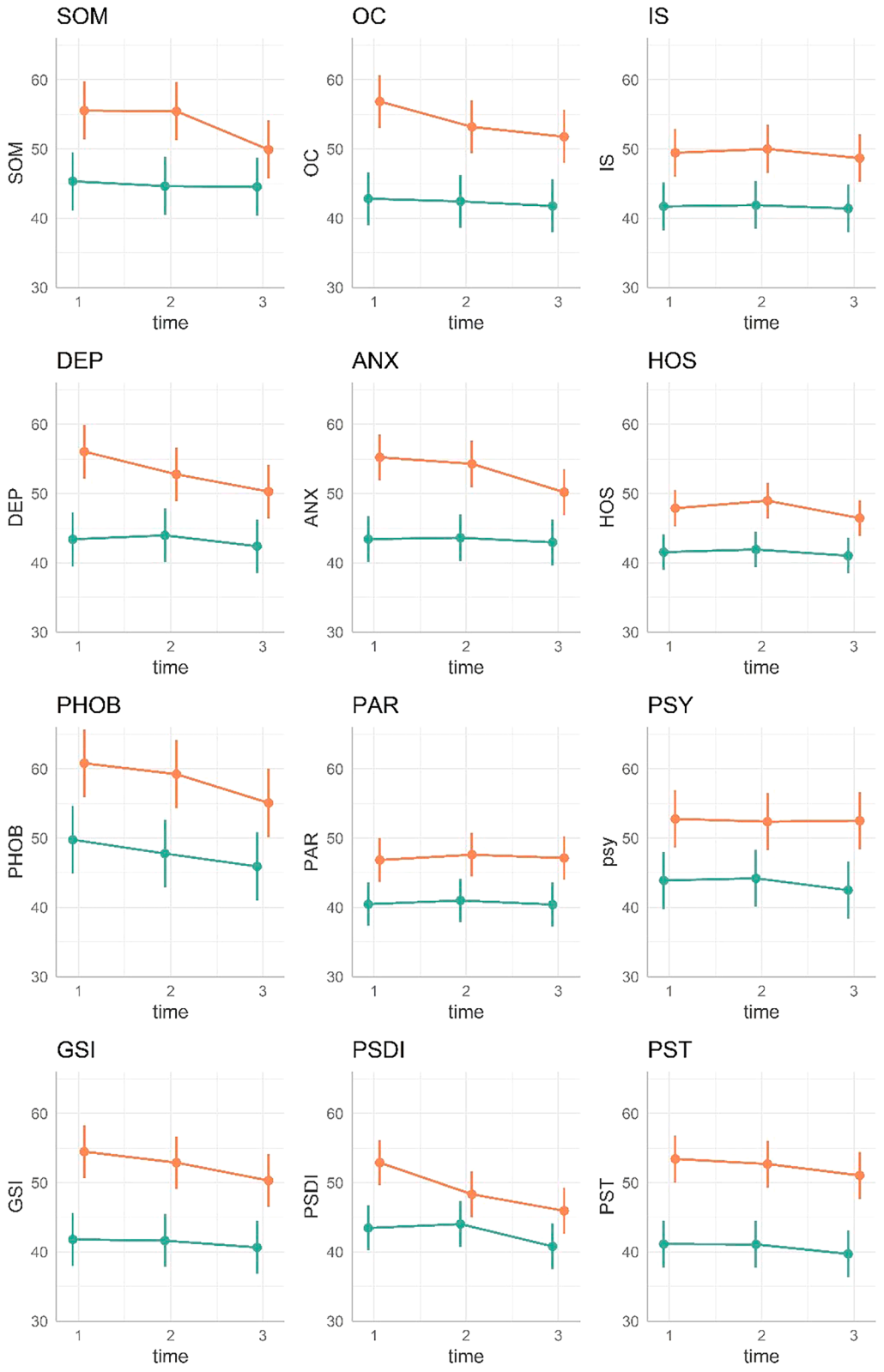

Fig. 1. Graph of the predicted Symptoms Checklist-90-Revised scores across trauma groups over time: 'trauma' group in red above, 'no trauma' group in light-blue below.

Note. The vertical bars are the 95% confidence intervals of the estimates. All subjects (n 70) have complete observations (n 210) across the three time points. PCL = Post-traumatic Stress Disorder Checklist; SOM = Somatization; OC = Obsessive-Compulsive; IS = Interpersonal Sensitivity; DEP = Depression; ANX = Anxiety; HOS = Hostility; PHOB = Phobic Anxiety; PAR = Paranoid Ideation; PSY = Psychoticism; GSI = Global Severity Index; PST = Positive Symptom Distress Index; PST = Positive Symptom Total.

[-9.29, -1.00], $p_{adj} = .031$). When the interaction of time and trauma is significant, it means that the 'trauma' group and the 'no trauma' group showed different patterns of change over time in the dependent variables; specifically, the 'trauma' group recovered slower than the 'no trauma' and thus had higher clinical scores on the SCL-90-R (see Fig. 1).

Conversely, such interaction of trauma(yes) and time (t1, t2, t3) was not statistically significant in influencing the scores of SOM, IS, HOS, PHOB, PAR, PSY, GSI, and PST – nor when comparing time 2 *vs* time 1 or time 3 *vs* time 1 (all $p_{adj} > .05$), meaning that the 'trauma' group and the 'no trauma' group did not change with statistically significant differences over time in these variables.

Summarizing the results across the models, trauma had a statistically significant effect in predicting worse outcomes for the 'trauma' group (i.e., the principal fixed effect of trauma) for all the SCL-90-R scales; moreover, the symptoms levels decrease over time, but some scales (e.g., depression, anxiety, obsessive-compulsive) decreased in a slower way for the 'trauma' group when comparing time 3 *vs* time 1 (i.e., the interaction effect of trauma*time). As for other scales (psychoticism, paranoid ideation, phobic anxiety, interpersonal sensitivity, hostility), the two groups did not show different trajectories over time with low and stable scores.

Discussion

The present findings provide a preliminary and original contribution to shed light on the psychological characteristics associated with the long-COVID disease. Experiencing COVID-19 illness as traumatic had a statistically significant worsening effect in influencing the course of psychopathological variables (i.e., higher scores on all SCL-90-R scales) up to 6 months after the first negative swab. In fact, patients reporting a traumatic experience during hospitalization, when compared to participants who did not, showed higher levels in all the measured psychological symptoms. At the same time, all the scales measuring psychological symptoms showed a decreasing trend over time, showing the progressive reduction of adverse symptoms over time. Although these findings nicely inform extant literature in the field, they should be cautionary interpreted, considering that the previous psychological conditions and mental health history of these participants are unknown.

Importantly, individuals without a provisional trauma diagnosis exhibited relatively low and stable scores over time. In contrast, those with a provisional trauma diagnosis followed a different trajectory over time, particularly on the scales of depressive, anxious, and obsessive-compulsive symptoms, which are able to capture these state-like variations over time. Specifically, the scores of the 'trauma' group were higher at time 1 and time 2, but reduced by time 3, converging toward lower symptomology and aligning with the 'no trauma' group. As the 'trauma' group did not undergo any planned treatment, the observed reduction in symptomatology may indicate a spontaneous recovery trajectory and/or psychological adaptation towards resilience (Bennett et al., 2023).

Anxiety and depression were among the most influenced psychological aspects during the pandemic (Zhu et al., 2022) – and they are the psychopathological features most involved during the experience of illness in general (Clarke & Currie, 2009; Cosci et al., 2015). On the one hand, higher anxiety levels can be explained by the anticipatory fear of the future, viewed as uncertain and/or negative, also with specific concerns about physical health (Bottesi et al., 2022; Freeston et al., 2020). On the other hand, depressive symptoms may reflect the mood deflection typical of the psychological response to prolonged and/or extremely stressful conditions – as a life-threatening illness (Lazarus, 1974). Additionally, depressive symptoms could be the result of other adverse emotions (e.g., fear) or trauma itself (Rossi et al., 2020; Rossi, Panzeri, Taccini, et al., 2022). When it comes to the obsessive-compulsive symptoms, their increased levels can be explained by at least two reasons. Firstly, from a psycho(patho)logical point of view, when individuals are facing an unpredictable, scaring, and uncontrollable situation as a severe illness, they may easily feel to lack control over their condition, with the resulting psychological discomfort. At this point, obsessive-compulsive thoughts and behaviors offer an easy – yet dysfunctional – way to feel in control of their own life and condition, apparently and temporarily reducing the sense of discomfort (Moulding & Kyrios, 2007). Secondly, the COVID-19 containment measures may have exacerbated obsessive-compulsive symptoms, especially in individuals who were already more prone to them (e.g. with contamination fears), also in the general population (Bennett et al., 2023; Shafran et al., 2020). Moreover, the OC scale of the SCL-90-R also captures the subjective cognitive complaints, such as difficulties in concentration or memory, which are quite common among patients with long-COVID, and that may be the long-term result of both physical (e.g., fatigue) and psychological conditions (e.g., worries) (Cougle et al., 2007).

Interestingly, the trajectories of somatic symptomatology were not different between the two groups, but somatic symptoms sensibly decreased in the 'trauma' group from the third to the sixth month. However, it is worth noting that the contents covered by the SCL-90 somatic scale overlap and mingle with the physical symptoms of the COVID disease itself (e.g., item #48: short of breath; item #14: feeling weak). Therefore, being entangled with the physical symptoms of the disease, it is not suitable for reliable interpretations regarding psychological distress.

Furthermore, both groups did not show different trajectories over time in the specific scales of interpersonal sensitivity (IS) (e.g. item #41: feelings of inferiority), hostility (HOS) (e.g. item #63: violent impulse discontrol), paranoid ideation (PAR) (e.g. item #18: distrustful feelings), psychoticism (PSY) (e.g. item #16: auditory hallucinations), and phobic anxiety (PHOB) (e.g. item #13: agoraphobia) (all $p > .05$). The reason for this can be attributed to two sets of factors, both clinical and psychometric. From a clinical perspective, these scales are more associated with stable and trait-like constructs, often linked to personality. By definition, they are unlikely to undergo dramatic changes, neither with the onset of the disease nor in the relatively short period after it (6 months), especially without any targeted intervention. From a psychometric perspective, these scales exhibited low normal levels from the beginning, thus a further decrease would have been implausible.

Regarding the global indices (secondary outcomes), the trauma groups showed different trajectories over time only in the intensity of symptoms (PSDI global scale) but neither in the mean general distress (i.e., GSI) nor in the breadth of the symptoms (i.e., number of symptoms captured by the PST), suggesting that in this particular population the severity of the distress rather than its pervasiveness may assume greater relevance.

Summarizing, these findings suggest that a notable percentage of individuals hospitalized for COVID-19 may encounter psychiatric symptoms up to 6 months following the infection.

Despite being sometimes dysfunctional, these trajectories are also within the expected process of psychological reaction and adaptation to illness (Lazarus, 1974). Furthermore, it is important to remember that psychopathological symptoms, despite indicating psychological suffering, may also have a subjective and adaptive meaning because they represent the most functional response that an individual can provide at a given moment. For instance, anxious symptoms can prepare the individual for future challenges (Morris, 2019), obsessive-compulsive symptoms can reduce the discomfort associated with the lack of control over a situation (Moulding & Kyrios, 2007), and depressive symptoms can be a way to let the organism rest after a too intense psychological effort or to increase interpersonal support through social signaling (Constant et al., 2021).

The findings of the present research are in line with existing literature, both with single studies showing that trauma symptoms predict the presence of psychopathological symptoms (e.g., Poyraz et al., 2021) and with cumulative studies (e.g., Schou et al., 2021; Zeng et al., 2023). Also, these findings are consistent with previous research investigating the

mental health of survivors of other outbreaks – such as the severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) – who reported elevated rates of psychiatric morbidity ranging from 10% to 35% in the post-illness phase (Lee et al., 2018), even 12 months after the acute infection, with 42% of patients exhibiting symptoms of PTSD and 27% experiencing depression (Lee et al., 2019).

Regarding the prevalence of PTSD in patients hospitalized for COVID-19, the reported prevalence of post-traumatic stress symptoms (PTSS) is higher than the rates observed in the general population, where affected individuals typically range from 7% to 10% (Liu et al., 2020; Tan et al., 2020). According to metanalytic evidence, at the beginning of the pandemic the overall pooled prevalence of PTSS was 27% (95%CI [12%, 45%]) and varied across groups, with the highest burden in patients with COVID-19 (96%; 95%CI [95%, 97%]), followed by the general population (15%; 95%CI [4%, 31%]), and healthcare workers (13%; 95%CI [11%, 16%]) (Krishnamoorthy et al., 2020). After two years of pandemic, the pooled prevalence of PTSS among patients with severe COVID-19 was 16% (95%CI [9%, 23%]) (Nagarajan et al., 2022).

At the same time, it is worth noting that PTSD has been consistently reported during the pandemic as a result of living in a state of stress, uncertainty, and disruption of daily life rather than directly caused by the disease itself (Schou et al., 2021; Tan et al., 2020; Wang et al., 2020) and also surviving a critical illness has been shown to trigger symptoms of post-traumatic stress (Sparks, 2018). However, given the absence of a formal diagnostic process for PTSD, it is only possible to state that these patients showed high levels of post-traumatic symptoms and not a proper diagnosis by a clinician.

Limitations

It is important to consider some limitations of this study. The first is about the sample selection, since patients not completing all the assessment points (because of willingness or possibility) were excluded from the analysis. If all the patients had participated, the proportion of those with psychological sequelae could have been different. However, preliminary analyses showed that the excluded participants did not differ in terms of any relevant variable, except for variables associated with adherence to the longitudinal assessment (e.g. higher education) (Jankowsky & Schroeders, 2022). Secondly, the study also included self-report tools that have potential biases (e.g., social-desirability) (Paulhus & Vazire, 2005), and there was no diagnosis of PTSD through a clinician-administered tool (e.g., Structured Clinical Interview for DSM-5 or Clinician-Administered PTSD Scale for DSM-5), thus the trauma groups were created according to the provisional PTSD diagnosis by the PCL-5, which still showed good sensitivity and accuracy (Weathers et al., 2013). Additionally, ethnicity and socioeconomic status were not specifically considered even though people from minorities or disadvantaged groups may have undergone more severe circumstances (both physical and psychological) because of potential discriminations. To conclude, it is not possible to infer any causal association from the present observational study, as the previous psychological conditions (e.g., prior mental health history) of the participants are not known, and they did not undergo any experimental manipulation. Lastly, the possible role of not measured confounding variables (e.g., family status, social support, absolute time-related variations, potential non-controlled treatments, preexisting susceptibility to trauma) cannot be excluded. Future studies (e.g., RCTs) may overcome these limitations.

Strengths

The present research study also has some strengths, both clinical and methodological. Among the clinical strengths, there are the particularity of the clinical sample of COVID-survivors discharged from the hospital after severe COVID-19 disease, who were followed over time to describe the psychological characteristics and the related abovementioned novel findings. Among the methodological strengths, there are the longitudinal design with 3 assessment points over time (from the first negative swab to 6 months of follow-up) and the accurate and rigorous statistical analysis procedures. Another methodological strength consists in the thorough assessment procedure using psychometrically sound measurement scales. All the scales were validated in Italian and showed strong psychometric properties, including construct, structural, and external validity. Sound and valid measurements are considered crucial steps in enhancing the field of psychological science and mitigating the replicability crisis (Flake et al., 2017; Flake & Fried, 2020; Gelman, 2016).

Future research may use clinician-administered tools to evaluate the psychological and psychiatric symptoms over time. Cumulative studies as metanalyses are encouraged to synthesize the aggregate evidence emerging from single studies as the present one over time.

Further considerations and recommendations

The present research enriches and updates the current literature about the long-term psychological consequences of COVID. Indeed, on the one hand, a recent review addressed this topic (Zeng et al., 2023), but with a search up to September 2021. On the other hand, most of the pre-existing studies were cross-sectional and showed that long COVID is associated with elevated levels of depression (+13%), anxiety (+28%), suicidal ideation (+10%), and post-traumatic stress disorder (+20%), as well as a reduction in life satisfaction and daily functioning (Craparo et al., 2022; Goodman et al., 2023). Among the few longitudinal studies, most of them focused on the physical symptoms of long-COVID-19 rather than the psychological ones (e.g., Mohtasham-Amiri et al., 2023), or were conducted in the general population, as a recent panel study in a large sample from the United Kingdom (UK) (e.g., Bu et al., 2023) not considering trauma-related symptoms. Additionally, the present research examines a period of up to 6 months that is longer than similar studies (Gramaglia et al., 2021) relying on shorter periods (i.e., 3-4 months).

Moreover, in relation to the current scientific literature, most of evidence about the impact of COVID-19 found heightened levels of anxiety and depression. However, we believe that research should not solely focus on what already emerged, but keep a broad range of possibilities to explore (to avoid confirmation bias in research). Therefore, also measuring non-'mainstream' constructs is a resource in this sense. Still, a good measurement is the first step in evaluating a construct and learning more about it. In this study, depression and anxiety still were the constructs most impacted by the traumatic experiences related to COVID-19. This aligns with the current literature, but our findings also described the trajectories of a wide range of additional and relevant psychological and psychiatric constructs through the SCL-90-R. Despite not showing significant elevations, it is important to evaluate and monitor them longitudinally because of their involvement in the planning and implementation of clinical interventions. The latter is often focused on state-like symptoms such as anxiety and depression, but is also frequently hindered by inflexible personality traits.

Finally, an important and complex topic related to trauma is represented by trauma susceptibility factors (for a review, Bomyea et al., 2012). Beyond the scope of this study, disentangling the psychological impact of trauma itself or its susceptibility factors poses a real challenge for research. Trauma susceptibility factors encompass a broad variety of elements: biological, neuroendocrine, cognitive, psychological, genetic, and epigenetic ones (e.g., Daskalakis et al., 2018). Among the psychological factors that influence susceptibility to PTSD, there are not only manifest preexisting mental health diagnoses, but also subclinical transdiagnostic constructs, such as emotional regulation, negative attributional style, looming cognitive style (Beevers et al., 2011) and intolerance of uncertainty (Boelen, 2019; Oglesby et al., 2016). To date, due to methodological constraints, few longitudinal prospective studies

have investigated susceptibility to trauma, primary among military samples (e.g., van Zuiden, Geuze, et al., 2011; van Zuiden, Kavelaars, et al., 2011). The topic of trauma susceptibility serves as a reminder for scientific research concerning the complex interplay of factors that interact at different levels to influence mental health outcomes. At the same time, it also acts as a stimulus for progress and the continued expansion of knowledge.

Conclusions

Traumatic experiences may play an important role in shaping the psychological conditions related to long-COVID, influencing their pattern up to 6 months after the first negative swab. Thus, in medical contexts dealing with physical illness – such as COVID-19 and its post-acute form – it is important to evaluate whether the individual experience is traumatic or not in order to tailor and program clinical interventions and to facilitate the allocation of resources over time, to promote psychological health and well-being. Ensuring timely and suitable prevention and intervention measures is crucial to prevent long-term adverse consequences and to promote the overall physical and mental health of individuals who have survived COVID-19 and are dealing with the long-COVID psychological correlates.

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CRediT authorship contribution statement

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Declaration of Competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2023.115609.

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