



Short Communication

Changes in Private Psychiatric **Outservice Related to SARS-CoV-2 Pandemic**

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Abstract

The SARS-CoV-2 pandemic, which began in late 2019, initially manifested with acute respiratory symptoms, including bilateral pneumonia, and later emerged as a systemic disease. This brief report assesses changes in the clinical profiles of psychiatric outpatients before, during, and after the pandemic's most severe periods, focusing on mood, anxiety, and cognitive symptoms. Data from a private psychiatric facility in Rome reveal that both pandemic-related stressors and SARS-CoV-2 infection itself may contribute to enduring affective and cognitive symptoms in both older and younger adult subgroups. Notably, during the pandemic, older patients showed elevated psychopathology scores (BPRS-24) compared to younger individuals. In the post-pandemic period, younger adults exhibited increased positive symptoms on the PANSS Positive subscale, suggesting a gradual worsening in symptoms post-pandemic (p = 0.47). Cognitive assessments (MMSE and PM38) further highlighted fluctuating performance over time, with older adults showing two distinct declines during the pandemic and in 2024. This work underscores the importance of sustained mental health interventions to address the pandemic's psychosocial and neuroinflammatory legacy. This perspective also considers new data on the CNS effects of "toxin-like peptides" synthesized by microbiome bacteria.

More Information

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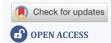
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Keywords: Outpatients psychiatric services; Clinical profile shifts; Neuro Covid; Long Covid; Age differences



Introduction

The SARS-CoV-2 pandemic, which originated in late 2019, rapidly spread worldwide in 2020, leading to widespread COVID-19 cases characterized initially by severe acute respiratory symptoms and bilateral pneumonia (SARS). However, COVID-19 was soon recognized as a systemic pathology, with Disseminated Intravascular Coagulation (DIC) often contributing to fatal outcomes, likely associated with inflammatory mechanisms triggered by the viral spike protein.

Among the systems notably affected by SARS-CoV-2 infection was the central nervous system, with symptoms such as anosmia, headache, and cognitive and affective disturbances [1,2]. The course of the disease included a critical 2–3-week period, after which survivors typically experienced resolution within a few weeks. However, many individuals continued to suffer from a persistent syndrome, commonly termed Long COVID [3,4], marked by fatigue, affective symptoms, and cognitive impairments [5].

Four years after the most acute pandemic period, residual symptoms in some individuals have become increasingly characterized as psychiatric and neurological. In July 2024, Taquet, et al. [6] published a follow-up study examining cognitive and psychiatric outcomes in 475 individuals $(40.2\% \text{ women}, 59.8\% \text{ men}; \text{ mean age} = 58.26 \pm 11.13 \text{ years})$ previously hospitalized for COVID-19. Cognitive scores for participants were 0.71 SD below expected values based on their sociodemographic characteristics across all cognitive domains tested. Most participants reported at least mild depression (74.5%), mild anxiety (53.5%), mild fatigue (62.3%), or mild subjective cognitive decline (52.1%). Over one in five participants reported severe depression (22.4%), severe fatigue (24.6%), or severe subjective cognitive decline (24.9%).

Most existing studies have focused on groups of COVID-19 survivors. However, no studies have assessed the pandemic's impact on the general psychiatric outpatient population, whether due to infection or the associated psychosocial stressors on a global level.

This report examines changes in the clinical profiles of psychiatric outpatients seeking consultations during the pandemic compared to those in the pre-and post-pandemic periods.



Material and methods

Data were collected from a private psychiatric outpatient facility in Rome, Italy, during each patient's first consultation with a specialist. Subjects were not pre-selected based on SARS-CoV-2 infection status; they were included based solely on their consultation request.

All subjects have signed an informed consent to have data electronically recorded, which can be included anonymously in a clinical study for scientific purposes and quality improvement.

Data include clinical assessments conducted by a single specialist using Key's Positive and Negative Symptoms Scale (PANSS) and Ventura's 24-item Brief Psychiatric Rating Scale (BPRS). Patients also self-reported depressive symptoms on the Rome Depression Inventory (RDI).

This naturalistic retrospective study compares patient profiles from the pre-pandemic (2018–2019; N = 127), pandemic (2020–2021; N = 130), and post-pandemic (2022–2023; N = 189) periods. Data from the first half of 2024 were also analyzed (N = 52). The data were split into two age-based subgroups.

In England's REACT-2 Study (2020–2023), persistent symptoms after SARS-CoV-2 infection were more common in individuals over 45 [7]. A later prevalence study (2023–2024) by the English Office for National Statistics found an elevated risk of persistent symptoms in individuals aged 35–65 [8]. For our study, we selected a threshold of 47 years, the median age of our sample, to divide participants into two roughly equal subgroups. This threshold aligns with the REACT-2 Study's findings and is close to the midpoint of the ONS study's highrisk range.

Statistical significance was assessed using 1-Way ANOVA for changes over time across the entire sample and each age subgroup, as well as for differences between groups across the four periods.

Results and discussion

Table 1 presents mean scores for the Positive subscale of Key's PANSS, showing significant differences in the overall sample (p = 0.023), though not within each age subgroup separately. BPRS scores, on the other hand, showed significant variations in both the overall sample (p = 0.037) and the older subgroup (p = 0.002). Mean scores from both scales are plotted in Figure 1. Significant differences between the two age groups appeared in the pandemic period and the two years following: older patients exhibited higher levels of psychopathology (BPRS24) during the pandemic compared to younger patients (p = 0.019), while younger patients exhibited higher levels of Positive Symptoms in PANSS in the two years after the pandemic (p = 0.047).

Table 2 and Figure 2 show mean scores on the RDI scale for depression. Significant changes were observed only in the younger subgroup (p = 0.006). The two subgroups showed different temporal trends: older patients experienced a slight increase in depressive symptoms during the pandemic, which then returned to pre-pandemic levels, while depressive symptoms in younger patients progressively increased over time.

As for cognitive functions, cognitive decline was observed as a prominent symptom of Long COVID. Assessments using MMSE and PM38 indicated significant variations, particularly in the older subgroup, with a reduction in PM38 (p = 0.047) and MMSE (p = 0.041) during the pandemic. In the two years following, this subgroup showed an initial recovery followed by another decline in early 2024 (Table 3, Figure 3). The younger group exhibited opposite trends, with significant differences from the older group during the pandemic (p(MMSE)=0.002; p(PM38)<0.001). In 2024, the divergence between the two groups re-emerged, particularly in PM38 scores (p = 0.005).

These findings provide insight into psychiatric outpatients' clinical profiles before, during, and after the pandemic. Observed changes suggest a potential direct and/or indirect impact of SARS-CoV-2 on this population, with two distinct symptom types (affective and cognitive) manifesting differently by age. Older patients exhibited greater mental distress, which appeared to diminish post-pandemic, while younger patients showed a progressive increase in depressive symptoms over time. Cognitive symptoms worsened over time in older patients, with two peaks—one during the pandemic and another in early 2024.

This study complements existing research by examining psychiatric outpatients rather than COVID-19-diagnosed individuals, broadening our understanding of the pandemic's population-level effects. Our findings support a double consequence of SARS-CoV-2 infection on mental health, as reported in previous studies: (1) a psychobiological response to pandemic-related stressors and lockdown measures, which may have synchronized mood disorders in some individuals; and (2) a cognitive component potentially linked to infection-induced neuroinflammatory processes, particularly in older individuals.

The persistent neuropsychiatric symptoms may represent manifestations of ongoing Long COVID (Neuro Long COVID). Amadoro, et al. [9] identified several risk factors that correlate cognitive impairment with COVID-19, highlighting shared biological mechanisms with other neurodegenerative diseases. Older individuals with pre-existing neuroinflammation may be at higher risk for cognitive decline following SARS-CoV-2 infection. Possible mechanisms for Neuro Long COVID include (1) cerebrovascular events related to altered blood coagulability, (2) encephalitis from a viral invasion of the CNS, (3) persistent inflammation mediated by microglia, and (4) individual predisposing factors.



Table 1: Included Subjects and Statistical Significance of Differences in PANSS-P and BPRS mean scores.

PANSS-P	Subgroup	2028-2019	2020-2021	2022-2023	2024 (6 months)	p(time)
m ±SD (N)	All	8.75 ± 2,3 (127)	9,13 ± 1,9 (130)	9,46 ± 2,2 (189)	9,52 ± 1,9 (52)	p = 0.023
	Age <47	8,93 ± 1,8 (55)	9,07 ± 1,9 (68)	9,75 ± 2,4 (104)	9,50 ± 2,1 (28)	ns
	Age >47	8,54 ± 2,6 (70)	9,21 ± 1,9 (61)	9,10 ± 2,0 84	9,54 ± 1,7 (24)	ns
	p(group)	ns	ns	p = .047	ns	
BPRS	Subgroup	2028-2019	2020-2021	2022-2023	2024 (6 months)	p(time)
	All	35,26 ± 5,2 (127)	36,96 ± 5,4 (130)	36,32 ± 4,9 (189)	37,06 ± 4,8 (52)	p = 0.037
m ±SD (N)	Age <47	35,71 ± 4,8 (55)	35,90 ± 5,6 (68)	36,63 ± 5,3 (104)	37,79 ± 4,4 (28)	ns
	Age >47	34,69 ± 5,4 (70)	38,13 ± 5,0 (61)	35,96 ± 4,5 (84)	36,21 ± 5,2 (24)	p = 0.002
	p(group)	ns	p = .019	ns	ns	

Abbreviations: PANSS-P: Positive and Negative Symptoms Scale – Positive Subscale mean score; BPRS: Brief Psychiatric Rating Scale (24 items) mean score; p(group): Statistical significance of differences observed in each time between age subgroups (shown on the correspondent line in each time column); p(time): Statistical significance of differences observed in all subjects or single age subgroup over time (shown in the last right column); ns: non significant; m: mean; SD: Standard Deviation; N: Number of Subjects.

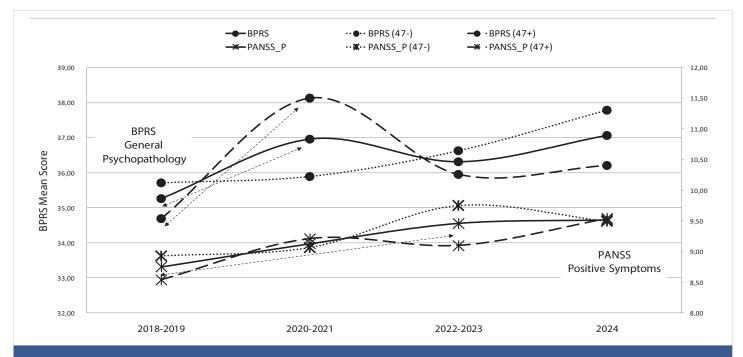


Figure 1: Changes in the mean score of the *Brief Psychiatric Rating Scale (24 items)* (BPRS; circles) and the *Positive and Negative Symptoms Scale – Positive Subscale* (PANSS_P; stars) in the two-year period pre-pandemic, pandemic, post-pandemic and in the first semester of 2024. The data are reported both in total (*solid line*) and divided into two age subgroups (over 47 years, *dotted line*, and under 47 years, *dashed line*); (47-): group aged under 47 years; (47+): group aged over 47 years; statistically significant differences between two different periods are reported (*dashed line with two arrows*). The observed population consists of the people at the first visit, seeking specialist support.

Table 2: Included Subjects and Statistical Significance of Differences in RDI mean T-scores.

RDI	Subgroup	2028-2019	2020-2021	2022-2023	2024 (6 months)	p(time)
m ±SD (N)	All	67,18 ± 16,3 (93)	68,66 ± 17,1 (106)	68,88 ± 15,0 (156)	74,44 ± 12,9 (39)	ns
	Age <47	64,07 ± 16,3 (45)	66,47 ± 15,0 (59)	69,10 ± 15,0 (87)	77,32 ± 9,9 (22)	p = 0.006
	Age >47	70,46 ± 16,0 (46)	72,11 ± 18,8 (46)	68,93 ± 14,8 (68)	70,71 ± 15,4 (17)	ns
	p(group)	ns	ns	ns	ns	

Abbreviations: RDI: Rome Depression Inventory mean T score (cut-off = 65); p(group): statistical significance of differences observed in each time between age subgroups (shown on the correspondent line in each time column); p(time): statistical significance of differences observed in all subjects or single age subgroup over time (shown in the last right column); ns: non significant; m: mean; SD: Standard Deviation; N: Number of Subjects.



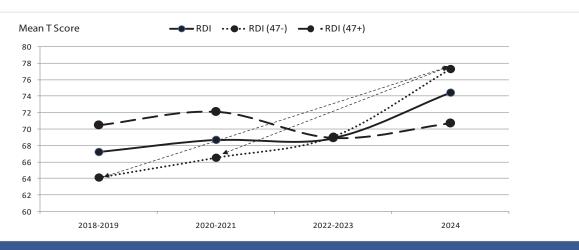


Figure 2: Changes in the mean score of the *Rome Depression Inventory* (RDI; circles) in the pre-pandemic, pandemic, post-pandemic two-year period and in the first semester of 2024. The data are reported both in total (*solid line*) and divided into two age subgroups (over 47 years, *dotted line*, and under 47 years, *dashed line*); (47-): group aged under 47 years; (47+): group aged over 47 years; statistically significant differences between two different periods are reported (*dashed line with two arrows*). Mean T Score: the mean score of RDI is expressed as T-score, where 50 is the mean, and 65 is the cut-off for pathology. The observed population consists of the people at the first visit, seeking specialist support.

ole 3: Included Su	bjects and Statistical Signi	ficance of Differences in MI	MSE and PM38.			
MMSE	Subgroup	2028-2019	2020-2021	2022-2023	2024 (6 months)	p(time)
m ±SD (N)	All	27,66 ± 2,7 (86)	27,00 ± 3,7 (100)	28,12 ± 2,3 (133)	27,14 ± 4,7 (42)	p = 0.048
	Age <47	28,24 ± 2,4 (38)	28,31 ± 2,3 (42)	28,35 ± 2,1 (69)	28,09 ± 2,2 (22)	ns
	Age >47	27,21 ± 2,9 48	26,05 ± 4,3 58	27,88 ± 2,6 64	26,10 ± 6,4 20	p = 0.041
	p(group)	ns	p = .002	ns	ns	
PM38	Subgroup	2028-2019	2020-2021	2022-2023	2024 (6 months)	p(time)
m ±SD (N)	All	41,84 ± 13,0 (87)	38,95 ± 12,0 (102)	40,86 ± 11,0 (139)	42,71 ± 9,7 (45)	ns
	Age <47	44,79 ± 11,0 (38)	45,59 ± 6,9 (44)	42,34 ± 12,0 (73)	46,37 ± 7,8 (24)	ns
	Age >47	39,55 ± 14,0 (49)	33,91 ± 12,0 (58)	39,21 ± 10,0 (66)	38,52 ± 10,0 (21)	p = 0.047
	p(group)	ns	p < .001	ns	p = .005	

Abbreviations: MMSE: Mini Mental State Examination mean score; PM38: Progressive Matrices 38 mean score; p(group): statistical significance of differences observed in each time between age subgroups (shown on the correspondent line in each time column); p(time): statistical significance of differences observed in all subjects or single age subgroup over time (shown in the last right column); ns: non significant; m: mean; SD: Standard Deviation; N: Number of Subjects.

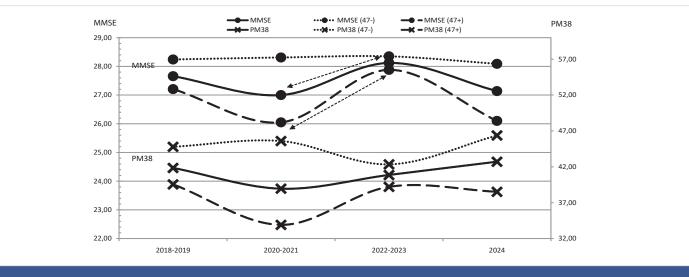


Figure 3: Changes in the mean score of the Mini Mental State Examination (MMSE; circles) and the Progressive Matrices 38 test (PM38; crosses) in the two-year period prepandemic, pandemic, post-pandemic and in the first semester of 2024. The data are reported both in total (solid line) and divided into two age subgroups (over 47 years, dotted line, and under 47 years, dashed line); (47-): group aged under 47 years; (47+): group aged over 47 years; statistically significant differences between two different periods are reported (dashed line with two arrows).



Exploring Neuro Long COVID's underlying mechanisms, Brogna, et al. [10] identified "toxin-like peptides" in COVID-19 patients, which are almost identical to components of animal venoms, such as conotoxins and phospholipases. These peptides, produced by gut bacteria, persisted even after SARS-CoV-2 RNA was undetectable [11]. Such findings may have implications for clinical symptom changes observed in psychiatric outpatients during the pandemic, suggesting an interaction between gut microbiota, SARS-CoV-2 variants, and individual risk factors, warranting a multidisciplinary approach.

Conclusion

Observations from psychiatric outpatient data suggest that patients' clinical profiles have shifted in association with the pandemic. Some changes, such as mood disturbances, appear linked to pandemic-related stressors, while others, particularly cognitive symptoms, may have different causes, such as age-related risk factors and potential microbiota interactions with SARS-CoV-2. These findings underscore the need for continued research into the neuropsychiatric impacts of SARS-CoV-2 and call for a comprehensive, multidisciplinary approach to managing these long-term effects.

Acknowledgement

The data are collected in anonymous indexed records, in a structured clinical practice, with previous informed consent of the patients. Structured clinical practice uses psychometrics instruments in everyday clinical practice to increase the quality of professional assistance. We acknowledge the cooperation of patients in improving such quality in fulfilling the questionnaires and undergoing neuropsychological assessment when asked.

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