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The negative and positive symptoms in people suffering from schizophrenia during the COVID-19 pandemic: a systematic review and meta-analysis.

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Abstract

The pandemic had a significant impact on the physical and mental health of the world population. In this context, higher levels of negative and positive symptoms related to psychosis have been observed. The present study aimed to verify, through a systematic review and meta-analysis, the evolution of negative and positive symptoms of schizophrenia during the pandemic period. The present work adhered to the PRISMA guidelines, and the GRADE and New Castle Ottawa bias scales were applied. Longitudinal studies from 2020-2021 that assessed negative and/or positive symptoms in persons diagnosed with schizophrenia before and during the pandemic period were searched on PubMed, PsycInfo and PsycArticles. The main results showed significant differences between the pre- and the pandemic period regarding negative symptoms [*average effect size* = -.47, *95% CI* ;-0.70, -0.24; $Z = 4.01$, $p < 0.0001$]. In conclusion, the work showed a worsening of negative symptoms during the pandemic in persons with schizophrenia. The results suggested the importance, in the post-pandemic period, of planning psychosocial interventions for these individuals.

Keywords: COVID-19; pandemic; schizophrenia; psychotic symptoms.

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Introduction

The Coronavirus Disease 2019 (COVID-19) caused a significant health impact on the global population (World Health Organization, 2020). Social distancing and impaired daily experiences during the pandemic period appeared to be linked to adverse psychological effects such as the onset of symptoms related to psychosis, anxiety, depression, and stress (Păunescu et al., 2022). Moreover, some vulnerable categories such as people suffering from mood disorders, suicidal ideation, and psychopathological symptoms, showed a different attitude toward the pandemic experiences and restrictive measures (Ciacchella et al., 2022a; Ciacchella et al., 2022b; Del Casale et al., 2022).

In the context of such global emergency, the effort of the healthcare systems was focused on pandemic management, causing a significant reduction of the resources employed in the treatment of other diseases (Ciacchella et al., 2022a). Therefore, people with pre-existing diagnoses of mental disorders had their symptoms worsened due to the sudden reduction in access to usual treatment (Yao et al., 2022; Vindegaard & Benros, 2020; Caponnetto et al., 2021; Mourani, 2022).

Recent studies suggested that attention should be paid to the physical and mental health of people suffering from schizophrenia, who showed, during the pandemic, a particular vulnerability due the disruption and instability of daily life, and the limited opportunities to use services (Fonseca et al., 2020; Strauss et al., 2021; Mueller-Stierlin et al., 2022). Indeed, the policies adopted during the COVID-19 pandemic, such as social distancing, impacted people with schizophrenia, who already have social deficits, possibly leading to a more significant decline in social functioning (Strauss et al., 2021). Several psychosocial factors, such as stressful life events, were found as risk factors for both the onset and the exacerbation of psychotic symptoms (Quittkat et al., 2020; Fusar-Poli et al., 2017). In this regard, in a sample of outpatients with schizophrenia, it was found that negative symptoms, defined by the reduction or complete impairment of emotional and behavioural functions (American Psychiatric Association, 2013), increased during the pandemic (Strauss et al., 2021).

Noteworthy, negative symptoms usually precede the manifestation of positive symptoms, described as inappropriate phenomena in addition to normal experiences, such as delusions and hallucinations, and have a higher associated burden of illness in people with schizophrenic syndrome (Velligan & Rao, 2023; American Psychiatric Association, 2013). Interestingly, the treatment with steroids used in the pandemic context have been found associated with an increased risk of psychotic-like symptoms, such as deliriums and or hallucinations (Brown et al., 2020). Moreover, the pandemic period was found to promote a higher prevalence of psychotic symptoms during the lockdown (Valdés-Florido et al., 2020).

During the pandemic, the already overburdened healthcare system was faced with unexpected consequences on the mental health of psychiatric patients, adapting to contingent situations. It is necessary to deepen the knowledge of the specific trajectories of psychopathological evolution, in order to provide useful indications for specialists to deal with possible future emergencies, such as the one experienced, and to manage the post-pandemic consequences.

Considering the vulnerabilities of schizophrenic patients, to date, there is a need to clarify whether the negative and positive symptoms of schizophrenia increased during the pandemic. The aim of this systematic review and meta-analysis was to verify how the negative and positive symptomatology of schizophrenia evolved during this pandemic period. The main hypothesis was both symptomatologies worsened during the pandemic period.

Method

This study adhered to the preferred reporting items for systematic review and meta-analysis PRISMA guidelines (see Table 1s in the Supplementary Material). The present study was not pre-registered on PROSPERO.

Search Strategy

A literature search was conducted using PubMed, PsycInfo and PsycArticle databases. In accordance with the PICO framework (patient problem or population; intervention; comparison or control and outcome) the search strategies used the following keywords: (covid-19 or coronavirus or 2019-ncov or sars-cov-2 or cov-19) AND (schizophrenia or psychotic disorder or psychotic symptoms). The keywords were inserted in the database, considering all the research fields (title, abstract, and text). The literature search covered a period of publication from 2020 to 2021. The emerging records were analysed for title, abstract and full text. Moreover, the reference lists of all selected articles and relevant systematic reviews were manually screened to identify any further references for possible inclusion.

Inclusion criteria

Only original research articles published from 2020 to 2021 were considered for inclusion in the systematic review and the meta-analysis. The inclusion criteria for the studies were: 1) to include patients with an established diagnosis of schizophrenia older than 18 years of age; 2) to include longitudinal articles with the assessment of the negative and/or positive symptomatology in pre-pandemic period (T0) *vs.* post-pandemic period (T1); 3) to provide means and standard deviation for quantitative analysis.

Exclusion criteria

Case reports, studies that included psychological intervention, studies not written in English language, and studies not conducted on humans were excluded.

Study selection

Following the search and exclusion of duplicates, three reviewers (authors GV, FL and MM) independently screened

the eligibility of the articles first on the title and the abstract, and on the full text according to the inclusion criteria. Disagreements were resolved by reviewer CC. According to the best practices for conducting a systematic review (Smith et al., 2011), the review team included at least one person with methodological expertise in conducting systematic reviews (CC) and at least one expert on the topic under review (VC).

Data extraction and synthesis

Authors MM, GV, FL independently extracted the following data from the included studies: authors and year of publication, Country, aim of the study, research design, sample, measures, and principal results (Appendix A of the Supplementary data, Table 2s) The two reviewers discussed any discrepancies and, if necessary, consulted a third team member (author CC) to reach a final decision.

Data Analysis

For the systematic review, a comparative table (Table 1) was created to count the frequencies of an improvement, worsening or nonsignificant change in the negative and positive symptoms of schizophrenia. Qualitative analysis was conducted by considering the number of studies, the number of samples, the total number of participating subjects, and the number of trials (each sample associated with a specific outcome related to negative and/or positive symptoms) in which there was an improvement, worsening or nonsignificant change in symptoms. The Review Manager Program 5.4 was used for the meta-analysis, in which the data on means and standard deviations and the total number of participants were considered for each sample. The comparison was conducted on the negative and positive symptoms, comparing the levels of symptomatology reported before COVID-19 and during COVID-19.

Standardized means differences were computed using a random effects model with 95% confidence interval. The I^2 value was used to evaluate the heterogeneity of the studies (I^2 < 50% acceptable and I^2 > 50% high). In the case of high heterogeneity, where the number of available studies allowed, it was planned to perform sensitivity analyses by differentiating the analyses conducted by sex and by the specific type of symptom detected (e.g., anhedonia, abolition). A minimum of two studies was required to perform the sensitivity analysis.

Assessment of bias risk, publication bias and GRADE

The present study adhered to New Castle Ottawa bias scale (Wells et al., 2000) (Appendix A of the Supplementary data, Table 3s) for the quality of observational studies. Assessment was conducted independently by author VC and GF and any disagreements resolved by a third author CC. In addition, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to rate the quality of evidence of the meta- analytic results (Appendix A of the Supplementary data, Table 4s). Quality of evidence was classified as high, moderate, low, or very low. GRADE uses a baseline rating of high for randomized controlled trials (RCTs) and low for non-RCTs. This rating can be downgraded or upgraded according to five assessment criteria, including risk of bias, inconsistency of results, indirectness, imprecision, and publication bias. Ratings were conducted by two authors (CC and MM).

Results

Studies selection

Electronic database searches identified 883 records (Fig. 1) of which 235 studies were excluded because they were not in English or not conducted on humans. The remaining 648 articles were evaluated for inclusion from the title and abstract, resulting in the exclusion of 621. The remaining 27 articles were evaluated for inclusion by reading the full text, resulting in the exclusion of 24 records. Finally, 3 observational studies were included in the systematic review and 2 observational studies were included in the meta-analysis.

Identification of the included studies

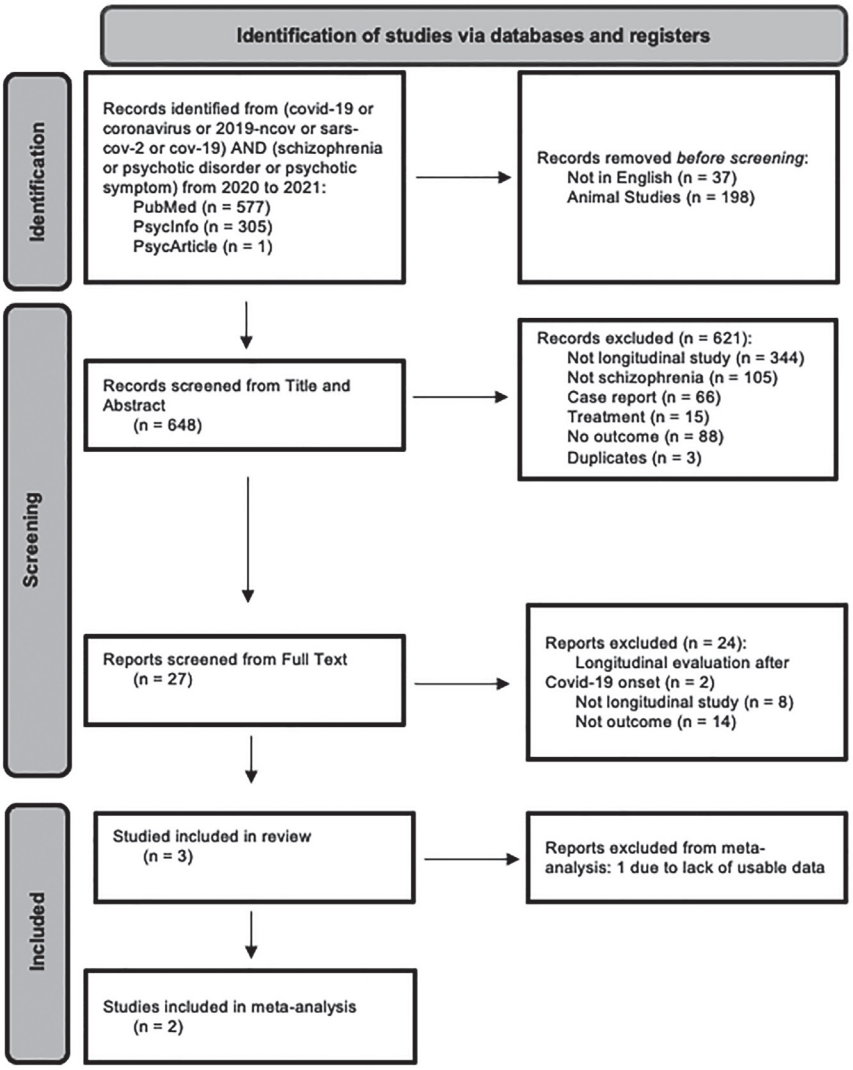
For the systematic review and meta-analysis, the identified studies were published between 2020 and 2021. In line with PICO framework, all the studies provided populations composed of women and men with a diagnosis of schizophrenia defined in the pre-pandemic period. All the studies reported useful data to compare the levels of symptomatology (negative or/and positive) at the pre-pandemic period *vs.* during pandemic period.

Tab. 1. Distribution of 10 trials (6 negative symptoms and 4 positive symptoms) coming from 130 samples of the 3 studies included in the systematic review.

Negative symptoms (6 trials)																		Positive symptoms (4 trials)											
Blunted affect			Anhedonia			Avolition			Asociality			Alogia			Deflated humor			Auditory hallucinations			Intrusive thinking			Perceptive alteration					
+	-	n.s	+	-	n.s	+	-	n.s	+	-	n.s	+	-	n.s	+	-	n.s	+	-	n.s	+	-	n.s	+	-	n.s			
	Strauss (2021)			Strauss (2021)			Strauss (2021)			Strauss (2021)			Straus (2021)			Pinkham (2020)			Quittkat (2020); Pinkham (2020)			Quittkat (2020)			Quittka (2020)			

Note: + improvement; - worsening; n.s no-significant changes.

Fig.1 Flow chart of the research, screening, and inclusion of the studies.



Characteristics of the included studies in the systematic review

The systematic review included 3 observational studies, with 3 experimental samples and 10 trials, including 6 trials for the negative symptoms and 4 trials for the positive symptoms. The total number of participants was 130. The measurement instruments used for the assessment of negative symptomatology are The Brief Negative Symptom Scale (BNSS, Kirkpatrick et al., 2010) and the Ecological Momentary Assessment (EMA, Pinkham et al. 2020). The measurement tools used for the assessment of positive symptomatology are the EMA (Pinkham et al., 2020) and the Continuum of Auditory Hallucinations-State Assessment (CHASA, Schlier et al., 2017). The table with the description of the included studies was reported in the supplementary materials (see Table 4s).

The three studies included in the systematic review showed the following results (see Table 1). In 4/6 trials, the negative symptomatology worsened during the pandemic compared with the pre-pandemic period (1 trial anhedonia, 1 trial avolition, 1 trial asociality, and 1 trial alogia). In 2/6 trials, the negative symptomatology reported nonsignificant changes between pre and during the pandemic period (see table 1). In 4/4 trials the positive symptomatology did not report significant changes between the pre and during the pandemic (see Table 1).

Characteristics and results of the included studies in the meta-analysis

Due to the reduced number of the eligible studies, the present meta-analysis should be interpreted as explorative. Indeed, only two observational studies were included, for a total of 2 experimental samples and 6 trials. The total number of participants was 124. The measurement instruments used to assess the negative symptomatology were the BNSS and the EMA.

The preliminary results showed significant differences between pre and during pandemic period on the negative symptomatology [*95% CI:* -0.47 (-0.70, -0.24); *Heterogeneity* Tau^2=0.03; Chi^2 = 7.66, df = 5, p = 0.18); I^2 = 35%; Z = 4.01, p < 0.0001].

The forest plot of the meta-analysis was reported in the supplementary materials (see Figure 1s).

Bias analysis, publication bias and GRADE assessment

The overall quality of the studies included was assessed through the New Castle Ottawa scale (see supplementary materials, Table 3s). The analysis shows that the studies considered are poorly representative of the schizophrenic population because of the small number of participants. Moreover, only self-report measures and observational studies are used for the assessment of the outcomes of interest. The completeness of longitudinal evaluations was found to be adequate.

Lastly, GRADE for the observational studies included was low (see Table 4s in the Supplementary Data).

Discussion

The aim of the present study was to examine the evolution of symptomatology in individuals with schizophrenia, comparing the levels of positive and negative symptomatology in the pre pandemic period with those occurred in the pandemic period.

The main hypothesis, that both positive and negative symptoms worsened during the pandemic period, was only partially confirmed. Indeed, the main results of the present study showed that there was a significant worsening of negative symptoms during the pandemic period. Both the systematic review and the meta-analysis conducted showed that the levels of severity of anhedonia, avolition, asociality, and alogia were significantly higher during the pandemic than in the pre-pandemic period. On the contrary, the positive symptoms did not change significantly.

It may be assumed that the significant worsening of negative symptoms is a consequence of the preventive measures taken against COVID-19. In this context, although restrictive measures have proven to be the most effective in controlling the spread of the virus (Khanna et al., 2020; Girum et al., 2021), the reduced frequency of social interactions, and the difficulty in pursuing recreational and daily activities may have contributed to the exacerbation of negative symptoms (Strauss et al., 2022). Coherently, environmental deprivation factors and impoverished social interactions have previously been associated with the severity of negative symptoms in hospitalised patients with schizophrenia (Oshima et al., 2005). Moreover, it should be considered that, in the last 3 years, people suffering from schizophrenia may have encountered barriers to usual therapeutic care, having difficulty in accessing psycho-social treatment (Byrne et al., 2021; Orrù et al., 2020; Szkody et al., 2020; Yao et al., 2022). Psycho-social care appeared to have a positive effect on functioning and danger of relapse of these vulnerable individuals (Ventriglio et al., 2020). These types of interventions seemed to be particularly outlined for the management of the anhedonic symptoms, of the social withdrawal, and affective flattening (Ventriglio et al., 2020).

In contrast to the initial hypotheses of the present study, the results showed that the positive symptoms did not appear to be changed during the pandemic period. This finding emerged from the systematic review, as a meta-analysis could not be performed due to a lack of useful data. In this regard, it should be noted that the present study focused on data collected when the pandemic was in its acute phase. It has been proposed that negative symptoms such as anhedonia, asociality, avolition and alogia often precede the manifestation of positive symptoms (Velligan & Rao, 2023). In this regard, it would be interesting to verify whether the positive symptomatology increased in the post-pandemic period..

Furthermore, there should be evidence that pharmacological interventions have a greater effect on positive symptoms than on negative ones (Leucht et al., 2013). It can be assumed that the treatment of the acute phase of psychosis was kept constant even during the pandemic period, ensuring the stability of positive symptomatology. Interestingly, the stability of drug treatment seemed to be guaranteed by the constant use of telepsychiatry, which provided remote psychiatric care through technology (Byrne et al., 2021). Consistently, a recent study found that antipsychotic drugs remained constant during the pandemic (Zhdanava et al., 2022). This is particularly relevant as the adherence to antipsychotic helped to achieve positive outcomes for psychotic symptoms, protecting against adverse courses of positive symptoms (Schlosser et al., 2015).

Despite the interesting findings of the present study, some limitations should be highlighted. Firstly, this work was not pre-registered, as PROSPERO is a prospective register and does not accept the submission of reviews that have started data extraction or have made further progress. At the submission stage of this work on PROSPERO, data had already been extracted. This is a relevant limitation since the pre-registration of a systematic review promotes transparency and helps authors to identify possible biases, anticipating methodological strategies.

Moreover, the literature included for the present systematic review, and particularly for the meta-analysis, considered only a limited number of studies, in which the described samples were not indicative of all people suffering from schizophrenia. Consequently, the results of this explorative meta-analysis should be intended as solely preliminary. Future studies should implement the sample to further investigate the possible clinical effects of the pandemic period in schizophrenia symptoms especially in the long term.

Furthermore, studies with more objective evaluations of the symptomatologic aspects of schizophrenia are required to precisely identify differences between negative and positive symptoms. In this regard, new studies should be planned using not only self-report measures but also objective measurement tools to assess all the variables of interest, such as clinical interview.

Despite the limitations mentioned above, the results of the present study give rise to some clinical implications. The COVID-19 pandemic seems to have influenced the worsening of negative symptoms rather than positive ones. This result could provide useful information in the event of new health emergencies, as it suggests that more resources should be invested in ensuring interventions that consider the negative side of psychotic symptomatology. In addition, the results of this study suggest that clinicians, in the presence of restrictive

measures, such as isolation, could use modern technologies to intervene not only on the positive symptoms of schizophrenia but also on the negative ones. Computer-mediated structured interventions could be a useful tool to implement the quality of life of people with severe negative schizophrenic symptomatology, as found by past studies (Hansson et al., 2008; Lawes-Wickwar et al., 2018).

Since the pandemic period seems to be drawing to a close, these results are relevant providing important insights for planning interventions aimed at mental health recovery. In this regard, interventions should focus more on treatments such as occupational therapies and psychosocial interventions, indicated to facilitate patients' reintegration into society and post-pandemic reality (Bassiony et al., 2022; Ventriglio et al. 2020; Yao et al., 2022). In addition, as high levels of burden were observed during the pandemic among caregivers of persons with schizophrenia (Yasuma et al., 2021), family interventions could be implemented to foster a better health-related quality of life for all family members (Caqueo-Urízar et al., 2021).

Author Contributions
The authors contributed equally to this manuscript.

Ethical Approval
Ethical approval is not required because this study retrieved and synthesized data from already published studies.

Conflict of interest
The authors declare that they have no conflicts of interest.

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Data availability
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Supplementary Material
Supplementary material are available at the following link: https://osf.io/fw9ha/?view_only=a5894515c8ce4e2e9af4efbbec2d58b6

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).

Bassiony, M. M., Sehlo, M. G., Ibrahim, E. F., Zayed, A. E., & Atwa, S. A. (2022). Assessment of compliance and relapse in patients with schizophrenia before and after the onset of COVID-19 pandemic. *International journal of psychiatry in clinical practice*, 1–7. Advance online publication. DOI: 10.1080/13651501.2022.2124175

Brown, E., Gray, R., Lo Monaco, S., O'Donoghue, B., Nelson, B., Thompson, A., Francey, S., & McGorry, P. (2020). The potential impact of COVID-19 on psychosis: A rapid review of contemporary epidemic and pandemic research. *Schizophrenia Research*, *222*, 79–87. DOI: 10.1016/j.schres.2020.05.005.

Byrne, A., Barber, R., & Lim, C. H. (2021). Impact of the COVID-19 pandemic – a mental health service perspective. *Progress in Neurology and Psychiatry*, *25*(2), 27. DOI: 10.1002/pnp.708

Caqueo-Urízar, A., Urzúa, A., Ponce-Correa, F., & Ferrer, R. (2021). Psychosocial Effects of the COVID-19 Pandemic on Patients With Schizophrenia and Their Caregivers. *Frontiers in Psychology*, *12*. DOI: 10.3389/fpsyg.2021.729793

Caponnetto, P., Benenati, A., & Maglia, M. G. (2021). Psychopathological Impact and Resilient Scenarios in patient with Schizophrenia Spectrum Disorders Related to Covid Physical Distancing Policies: A Systematic Review. *Behavioral Sciences*, *11*(4), 49. DOI: 10.3390/bs11040049

Ciacchella, C., Campedelli, V., Veneziani, G., Pellicano, G. R., Sambucini, D., & Lai, C. (2022a). Editorial: Impact of the Coronavirus Pandemic (COVID-19) on Mood Disorders and Suicide. *Frontiers in Psychiatry*, *13*. DOI: 10.3389/fpsyt.2022.846112

Ciacchella, C., Veneziani, G., Bagni, C., Campedelli, V., Del Casale, A., & Lai, C. (2022b). Escaping the Reality of the Pandemic: The Role of Hopelessness and Dissociation in COVID-19 Denialism. *Journal of Personalized Medicine*, *12*(8), 1302. DOI: 10.3390/jpm12081302

Del Casale, A., Lai, C., Iannuccelli, A., Ciacchella, C., Veneziani, G., Ali, M., Zocchi, C., Bilotta, I., & Pompili, M. (2022). Pandemic experiences and psychopathological aspects in individuals with mood disorders and other mental disorders. *Frontiers in Psychiatry*, *13*. DOI: 10.3389/fpsyt.2022.1039072

Fonseca, L., Diniz, E., Mendonça, G., Malinowski, F., Mari, J., & Gadelha, A. (2020). Schizophrenia and COVID-19: risks and recommendations. *Brazilian Journal of Psychiatry*, *42*(3), 236–238. DOI: 10.1590/1516-4446-2020-0010

Fusar-Poli, P., McGorry, P. D., & Kane, J. M. (2017). Improving outcomes of first-episode psychosis: an overview. *World Psychiatry*, *16*(3), 251–265. DOI: 10.1002/wps.20446

Girum, T., Lentiro, K., Geremew, M., Migora, B., Shewamare, S., & Shimbre, M. S. (2021). Optimal strategies for COVID-19 prevention from global evidence achieved through social distancing, stay at home, travel restriction and lockdown: a systematic review. *Archives of Public Health*, *79*(1). DOI: 10.1186/s13690-021-00663-8

Hansson, L., Svensson, B., Björkman, T., Bullenkamp, J., Lauber, C., Martinez-Leal, R., McCabe, R., Rössler, W., Salize, H., Torres-Gonzales, F., van den Brink, R., Wiersma, D., & Priebe, S. (2008). What works for whom in a computer-mediated communication intervention in community psychiatry? Moderators of outcome in a cluster randomized trial. Acta psychiatrica Scandinavica, 118(5), 404–409. DOI: 10.1111/j.1600-0447.2008.01258.x

Khanna, R., Cicinelli, M., Gilbert, S., Honavar, S., & Murthy, G. V. (2020). COVID-19 pandemic: Lessons learned and future directions. *Indian Journal of Ophthalmology*, *68*(5), 703. DOI: 10.4103/ijo.ijo_843_20

Kirkpatrick, B., Strauss, G. P., Nguyen, L., Fischer, B. A., Daniel, D. G., Cienfuegos, A., & Marder, S. R. (2010). The Brief Negative Symptom Scale: Psychometric Properties. *Schizophrenia Bulletin*, *37*(2), 300–305. DOI: 10.1093/schbul/sbq059

Lawes-Wickwar, S., McBain, H., & Mulligan, K. (2018). Application and effectiveness of telehealth to support severe mental illness management: systematic review. *JMIR mental health*, *5*(4), e8816. DOI: 10.2196/mental.8816

Leucht, S., Cipriani, A., Spineli, L., Mavridis, D., Örey, D., Richter, F., … & Davis, J. M. (2013). Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *The Lancet*, *382*(9896), 951-962. DOI: 10.1016/S0140-6736(13)60733-3

Mourani, S. C. (2022). Mechanisms of new-onset psychosis during the COVID-19 pandemic: What ignited the fire? *Annals of Clinical Psychiatry*, *34*(2). DOI: 10.12788/acp.0065

Mueller-Stierlin, A. S., Meixner, F., Lehle, J., Kohlmann, A., Schumacher, M., Woehler, S., Haensel, A., Reuter, S., Herder, K., Bias, N., Becker, T., & Kilian, R. (2022). Perceived empowerment and the impact of negative effects of the COVID-19 pandemic on the quality of life of persons with severe mental illness. *PLOS ONE*, *17*(10), e0276123. DOI: 10.1371/journal.pone.0276123

Oshima, I., Mino, Y., & Inomata, Y. (2005). Effects of environmental deprivation on negative symptoms of schizophrenia: a nationwide survey in Ja'an's psychiatric hospitals. *Psychiatry research*, *136*(2-3), 163-171. DOI: 10.1016/j.psychres.2005.06.001

Orrù G, Ciacchini R, Gemignani A, Conversano C. Psychological Intervention Measures During the Covid-19 Pandemic. *Clin Neuropsychiatry*. 2020 Apr;17(2):76-79. DOI: 10.36131/CN20200208

Păunescu, R. L., Miclu Ia, I. V., Verişezan, O. R., & Crecan-Suciu, B. D. (2022). Acute and longterm psychiatric symptoms associated with COVID19 (Review). Biomedical reports, 18(1), 4. DOI: 10.3892/br.2022.1586

Pinkham, A. E., Ackerman, R. A., Depp, C. A., Harvey, P. D., & Moore, R. C. (2020). A Longitudinal Investigation of the Effects of the COVID-19 Pandemic on the Mental Health of Individuals with Pre-existing Severe Mental Illnesses. Psychiatry research, 294, 113493. DOI: 10.1016/j.psychres.2020.113493

Quittkat, H. L., Düsing, R., Holtmann, F. J., Buhlmann, U., Svaldi, J., & Vocks, S. (2020). Perceived impact of Covid-19 across different mental disorders: a study on disorder-specific symptoms, psychosocial stress and behavior. Frontiers in Psychology, 11, 586246. DOI: 10.3389/fpsyg.2020.586246

Schlier, B., Hennig, T., and Lincoln, T. M. (2017). Measuring fluctuations across the continuum of auditory hallucinations. development and validation of a state inventory. Psychiatry Res. 253, 325–332. doi: 10.1016/j.psychres.2017.03.051 DOI: 10.1016/j.psychres.2017.03.051

Schlosser, D. A., Campellone, T. R., Biagianti, B., Delucchi, K. L., Gard, D. E., Fulford, D., Stuart, B. K., Fisher, M., Loewy, R. L., & Vinogradov, S. (2015). Modeling the role of negative symptoms in determining social functioning in individuals at clinical high risk of psychosis. *Schizophrenia Research*, *169*(1–3), 204–208. DOI: 10.1016/j.schres.2015.10.036

Smith, V., Devane, D., Begley, C. M., & Clarke, M. (2011). Methodology in conducting a systematic review of systematic reviews of healthcare interventions. BMC medical research methodology, 11(1), 1-6. DOI: 10.1186/1471-2288-11-15

Strauss, G. P., Macdonald, K. I., Ruiz, I., Raugh, I. M., Bartolomeo, L. A., & James, S. H. (2021). The impact of the COVID-19 pandemic on negative symptoms in individuals at clinical high-risk for psychosis and outpatients with chronic schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience*, *272*(1), 17–27. DOI: 10.1007/s00406-021-01260-0

Szkody, E., Stearns, M., Stanhope, L., & McKinney, C. (2020). Stress-Buffering Role of Social Support during COVID-19. *Family Process*, *60*(3), 1002–1015. DOI: 10.1111/famp.12618

Valdés-Florido, M. J., López-Díaz, Á., Palermo-Zeballos, F. J., Martínez-Molina, I., anMartín-Gil, V. E., Crespo-Facorro, B., & Ruiz-Veguilla, M. (2020). Reactive psychoses in the context of the COVID-19 pandemic: clinical perspectives from a case series. *Revista de psiquiatria y salud mental*, *13*(2), 90-94. DOI: 10.1016/j.rpsm.2020.04.009

Velligan, D. I., & Rao, S. (2023). Schizophrenia: Salient Symptoms and Pathophysiology. *The Journal of clinical psychiatry*, *84*(1), MS21078COM7. DOI: 10.4088/JCP.MS21078COM7

Ventriglio, A., Ricci, F., Magnifico, G., Chumakov, E., Torales, J., Watson, C., Castaldelli-Maia, J. M., Petito, A., & Bellomo, A. (2020). Psychosocial interventions in schizophrenia: Focus on guidelines. *International Journal of Social Psychiatry*, *66*(8), 735–747. DOI: 10.1177/0020764020934827

Vindegaard, N., & Benros, M. E. (2020). COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. *Brain, Behavior, and Immunity*, *89*, 531–542. DOI: 10.1016/j.bbi.2020.05.048

Wells, G. A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2000). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (2019), Accessed 31st January 2023

World Health Organization, 2020. Coronavirus Disease 2019 (COVID-19): Situation Report. p. 72

Yasuma, N., Yamaguchi, S., Ogawa, M., Shiozawa, T., Abe, M., Igarashi, M., Kawaguchi, T., Sato, S., Nishi, D., Kawakami, N., & Fujii, C. (2021). Care difficulties and burden during COVID-19 pandemic lockdowns among caregivers of people with schizophrenia: A cross-sectional study. *Neuropsychopharmacology Reports*, *41*(2), 242–247. DOI: 10.1002/npr2.12171

Yao, L., Liu, H., & Tian, X. (2022). Medication adherence among community-dwelling schizophrenia patients during the COVID-19 pandemic: A cross-sectional study. *Psychiatry research*, *317*, 114841. DOI: 10.1016/j.psychres.2022.114841

Zhdanava, M., Starr, H. L., Lefebvre, P., Totev, T. I., Shah, A., Sheng, K., & Pilon, D. (2022). Understanding the Health System Conditions Affecting the Use of Long-Acting Injectable Antipsychotics in the Treatment of Schizophrenia in Clinical Practice: A US Healthcare Provider Survey. *Neuropsychiatric Disease and Treatment*, *Volume 18*, 1479–1493. DOI: 10.2147/NDT.S369494