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Letter to the Editor

Lower risk of SARS-CoV2 infection in individuals with severe mental disorders on antipsychotic treatment: A retrospective epidemiological study in a representative Spanish population,



To the editors,

The population with severe mental disorders (SMD) is a medically and socially vulnerable group for a worse outcome in COVID-19. This population has been identified as high-risk group for COVID-19 due to lower awareness of risk, higher prevalence of cognitive impairment and who have limitations to maintain adequate barriers against virus propagation such as living in long-term care facilities, and people with underlying health conditions obesity, smoking, hypertension, diabetes as well as cardiovascular and respiratory diseases (Kozloff et al., 2020).

However, previous investigations to assess the prevalence of COVID-19 in SMD individuals have yielded to inconsistent results. Thus, Lee et al. (2020) reported that diagnosis of a mental disorder was not associated with increased likelihood of Severe Acute Respiratory Syndrome due to Coronavirus (SARS-CoV) infection, but was related to a slightly higher risk for severe clinical outcomes (Lee et al., 2020), whereas Wang and colleagues informed of an increased risk to be infected, especially those with a recent mental health diagnosis (Wang et al., 2020). On the other hand, a diagnosis of schizophrenia have been linked to increased risk for mortality (Nemani et al., 2021).

Antipsychotics seem to have a beneficial effect against MERS and SARS coronaviruses (Dyall et al., 2017). Interestingly, elopiprazole (a never marketed phenylpiperazine antipsychotic drug) was listed among the 21 most potent compounds to inhibit SARS-CoV infection (Riva et al., 2020) and chlorpromazine protects mice from severe clinical disease and SARS-CoV (Weston et al., 2020). We aimed to investigate the prevalence and prognosis of COVID-19 in an epidemiological cohort of SMD population who are treated with long-acting injectable (LAI) antipsychotic treatment.

An epidemiological retrospective study of SMD patients on LAI antipsychotic treatment with good treatment adherence (at least 80% of prescribed doses from March–November 2020) in the catchment area of the University Hospital Virgen del Rocío, Seville, Spain (encompassing a total population, older than 18 years, of 557.576 individuals) was carried out. A cohort of 698 individuals was analyzed. All procedures were in accordance with the Declaration of Helsinki. Ethical approval was obtained from the local Committee for Ethical Clinical Investigation (2578-N-2020). Prevalence information about infection, hospital and Intensive Care Unit (ICU) admission as well as death due to COVID-19 were displayed in Table 1. Clinical characteristics of SMD population are

summarized in Supplementary material.

Statistical analyses were conducted using SPSS, version 24. X^2 test or Fisher's exact test when expected cell counts were <5 were used to study whether the frequency of observations was significantly different between the general population and LAI users. The level of significance was set at 5%.

From February to November 2020 a total of 23,077 (4.1%) individuals were SARS-CoV-2 infected. Out of them, 9 SMD patients tested positive for COVID-19 (1.3%) of whom one (11.1%) was symptomatic (diarrhea). SARS-CoV-2 infection was confirmed in all the cases using the Polymerase Chain Reaction (PCR) test with an exception of one LAI user who was diagnosed by Antigen Test for SARS-CoV2 (See Table 1). Analyses revealed that a significantly reduced proportion of patients was infected by COVID-19 ($p \leq 0.001$). We also observed less proportion of hospital admissions (8.5% vs. 0%), ICU admissions (0.9% vs. 0%) and deaths (1.1% vs. 0%) due to COVID-19 although the differences were not statistically significant.

Counterintuitively, the main findings of the study were that vulnerable SMD individuals on antipsychotic treatment showed a lower risk of SARS-CoV2 infection and a likely better COVID-19 prognosis. It could be speculated that antipsychotics could play an important role preventing SARS-CoV-2 infection and may exert protective effects against detrimental courses of COVID-19. The results of the present study have to be taken judiciously, since not all the factors involved in the complex network of COVID-19 infection has been taken into account.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2021.02.002>.

Author's contributions

All the authors have participated and have made substantial contributor for this paper.

Ethical statement

Ethical approval was obtained from the Local Research Ethics Committee.

Table 1

COVID-19 clinical characteristics and outcome of SMD and non-SMD populations.

	SMD population (n = 698)	Non-SMD population (n = 557.576)
Infected, n (%)	9 (1.3%)	23,077 (4.1%)
Asymptomatic, n (%)	8 /9 (89%)	(–)
Hospitalizations ^a , n (%)	0/9 (0%)	1953/23077 (8.5%)
ICU admission, n (%)	0/9 (0%)	203/23077 (0.9%)
Deaths due to COVID-19, n (%)	0 (0%)	254/23077 (1.1%)
Age, mean (SD)	48.2 ± 12.7	(–)
Gender (male), n (%)	445 (63.8%)	(–)

SMD: severe mental disorder; ICU: intensive care unit.

(–) Accurate information is not available.

^a Due to medical condition related to COVID-19.

¹García-Sánchez, C.M, M.D., Martín-Gil, V.E, M.D., Arias Ruiz, A, M.D., Estévez-Martín, M, P.M.H.N.

Declaration of competing interest

The authors have no conflicts of interest concerning the subject of the study.

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References

- Dyall, J., Gross, R., Kindrachuk, J., Johnson, R.F., Olinger, G.G.J., Hensley, L.E., Frieman, M.B., Jahrling, P.B., 2017. Middle East respiratory syndrome and severe acute respiratory syndrome: current therapeutic options and potential targets for novel therapies. *Drugs* 77, 1935–1966. <https://doi.org/10.1007/s40265-017-0830-1>.
- Kozloff, N., Mulsant, B.H., Stergiopoulos, V., Voineskos, A.N., 2020. The COVID-19 global pandemic: implications for people with schizophrenia and related disorders. *Schizophr. Bull.* <https://doi.org/10.1093/schbul/sbaa051>.
- Lee, S.W., Yang, J.M., Moon, S.Y., Yoo, I.K., Ha, E.K., Kim, S.Y., Park, U.M., Choi, S., Lee, S.-H., Ahn, Y.M., Kim, J.-M., Koh, H.Y., Yon, D.K., 2020. Association between mental illness and COVID-19 susceptibility and clinical outcomes in South Korea: a nationwide cohort study. *Lancet Psychiatry* 7, 1025–1031. [https://doi.org/10.1016/S2215-0366\(20\)30421-1](https://doi.org/10.1016/S2215-0366(20)30421-1).
- Nemani, K., Li, C., Olfson, M., Blessing, E.M., Razavian, N., Chen, J., Petkova, E., Goff, D.C., 2021. Association of psychiatric disorders with mortality among patients with COVID-19. *JAMA Psychiatry*. <https://doi.org/10.1001/jamapsychiatry.2020.4442>.
- Riva, L., Yuan, S., Yin, X., Martin-Sancho, L., Matsunaga, N., Pache, L., Burgstaller-Muehlbacher, S., De Jesus, P.D., Teriete, P., Hull, M.V., Chang, M.W., Chan, J.F.-W., Cao, J., Poon, V.K.-M., Herbert, K.M., Cheng, K., Nguyen, T.-T.H., Rubanov, A., Pu, Y., Nguyen, C., Choi, A., Rathnasinghe, R., Schotsaert, M., Miorin, L., Dejoze, M., Zwaka, T.P., Sit, K.-Y., Martinez-Sobrido, L., Liu, W.-C., White, K.M., Chapman, M.E., Lendy, E.K., Glynn, R.J., Albrecht, R., Rupp, E., Mesecar, A.D., Johnson, J.R., Benner, C., Sun, R., Schultz, P.G., Su, A.I., García-Sastre, A., Chatterjee, A.K., Yuen, K.-Y., Chanda, S.K., 2020. Discovery of SARS-CoV-2 antiviral drugs through large-scale compound repurposing. *Nature* 586, 113–119. <https://doi.org/10.1038/s41586-020-2577-1>.
- Wang, Q.Q., Xu, R., Volkow, N.D., 2020. Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States. *World Psychiatry* <https://doi.org/10.1002/wps.20806>.
- Weston, S., Coleman, C.M., Haupt, R., Logue, J., Matthews, K., Li, Y., Reyes, H.M., Weiss, S.R., Frieman, M.B., 2020. Broad anti-coronavirus activity of Food and Drug Administration-approved drugs against SARS-CoV-2 in vitro and SARS-CoV in vivo. *J. Virol.* 94. <https://doi.org/10.1128/JVI.01218-20>.

M. Canal-Rivero
Hospital Universitario Virgen del Rocío, Sevilla, Spain
Instituto de Biomedicina de Sevilla (IBIS), Spain
Centro Investigación Biomédica en Red de Salud Mental (CIBERSAM), Spain

R. Catalán-Barragán
A. Rubio-García
Hospital Universitario Virgen del Rocío, Sevilla, Spain
Instituto de Biomedicina de Sevilla (IBIS), Spain

N. Garrido-Torres
Hospital Universitario Virgen del Rocío, Sevilla, Spain
Instituto de Biomedicina de Sevilla (IBIS), Spain
Centro Investigación Biomédica en Red de Salud Mental (CIBERSAM), Spain

B. Crespo-Facorro*
M. Ruiz-Veguilla
Hospital Universitario Virgen del Rocío, Sevilla, Spain
Instituto de Biomedicina de Sevilla (IBIS), Spain
Centro Investigación Biomédica en Red de Salud Mental (CIBERSAM), Spain

Departamento de Psiquiatría, Universidad de Sevilla, Spain
*Corresponding author at: Department of Psychiatry, University Hospital Virgen del Rocío, IBIS, CIBERSAM, School of Medicine, University of Sevilla, Spain.
E-mail address: benedicto.crespo.sspa@juntadeandalucia.es

IBIS Translational Psychiatry Group1

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