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Incidence and outcomes of COVID-19 first wave pandemic in a French nursing home with residents suffering from severe mental illnesses

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ABSTRACT

During the first wave of COVID-19, nearly 50% of France's fatalities occurred in nursing homes. Older people with mental health disorders are considered to be more prone to infections when epidemics arise. To test this hypothesis, we conducted a retrospective descriptive and comparative study of the incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a cohort of elderly residents with or without severe mental illness (SMI) living in a French nursing home facility. This was done during the first lockdown from March 17th until May 11th, 2020.

Our study included 72 participants of 75 residents, of whom 58 contracted COVID-19, 14 developed a severe form requiring hospitalisation, and 14 died. The disease was significantly less frequent in residents with SMI 15 (62%) than those without SMI 43 (89.6%). In regression analysis, a higher level of autonomy was significantly associated with a lower disease incidence. Once contracted, residents with or without SMI differed significantly neither on morbidity nor mortality. The period of survival did not either significantly differ between the two groups.

As a potential explanation, we suggested that pathological social withdrawal added to stigmatisation could have protected SMI residents from contracting the disease.

1. Introduction

On December 31st, 2019, The Wuhan Municipal Health Commission declared a pneumonia outbreak due to unknown causes (Lu et al., 2020). Less than a month later, a pathogen named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the source for coronavirus disease 2019 (COVID-19) (Sohrabi et al., 2020). On March 11th, the WHO declared the coronavirus outbreak a global pandemic (Cucinotta and Vanelli, 2020).

The first reported case in France occurred on January 24th, 2020 (Bernard Stoecklin et al., 2020). The infection rapidly spread afterwards, threatening to saturate resuscitation departments and disrupt healthcare services. To stem the outbreak, the French government introduced social restrictions (lockdown) from March 17th to May 11th, 2020. To date, 26,643 fatality cases were reported amongst 176,970 who tested positive for COVID-19. Nearly half of the fatalities occurred in the older age group in residential care facilities (Nicolas, 2020). French health authorities rapidly released guidelines to limit the SARS- CoV 2 transmission in these facilities, focusing on elderly suffering from severe mental illness (SMI, defined as schizophrenia or bipolar disorder). Older people with mental health disorders are more prone to infections when pandemics arise (Chevance et al., 2020). Possible explanations include cognitive impairment, little awareness of risk, and diminished self-protection efforts (Chevance et al., 2020).

Paradoxically, some clinical reports and epidemiological observations issued data suggesting a fewer incidence of COVID-19 in patients with severe mental illnesses, raising questions about protective demographical, immunological, or pharmacological factors (Plaze et al., 2020).

To test the hypothesis of a more significant occurrence of COVID-19 in the elderly with SMI, we conducted a study in a French residential nursing care facility where residents were either suffering from SMI or not. We compared potential risk/protective factors in both populations as a second step.

1.1. Description of the outbreak

On March 10th, the administrative supervisors of the X EHPAD

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implemented preventive measures. Residents were required to stay in their rooms and undergo assessments twice a day for possible signs and symptoms of COVID −19, notably fever, cough, and shortness of breath. Health care personnel were also assessed at the beginning of each shift. A week later, the national lockdown was enforced. Residents were restricted to their rooms, and all daily planned activities were suspended. The X EHPAD is a 75-bed medical skilled nursing home with five separate wings, A to E, each hosting an equal mix of SMI and non-SMI residents.

On March 21st, the first resident was tested positive in wing B. He was transferred to the hospital four days later and died twenty days after his diagnosis. The second case was reported on March 22nd in another wing; he died in the X EHPAD 15 days later. In the following weeks, 29 residents were diagnosed as COVID 19 on a clinical basis, of which 14 died.

During a survey carried out on April 21st, 55 residents underwent both PCR and serologic tests (three were hospitalised at that time with acute symptoms). Thirty residents were diagnosed with COVID-19, although asymptomatic. At the end of the study, 58 residents were diagnosed with COVID-19 either on a clinical or/and biological basis.

2. Methods

2.1. Study design and participants

We conducted a retrospective comparative epidemiological survey in EHPAD X, in Saint-Denis, a northern suburb of Paris, in France. The study was supported by the institutional review board. Written informed consent and participant anonymisation were required under the local research policy. Personal information processing was subject to a declaration to the French data protection agency.

There were 75 residents at the beginning of the study on March 17th, when the lockdown was first imposed. All residents, who provided consent (either directly or through their legal representative) to personal health data use, were included.

2.2. Data collections' procedures

We extracted data on clinical and demographic characteristics, laboratory findings, and therapeutics from the electronic health records during the study period, commencing March 17th ending May 11th, 2020.

2.2.1. Demographic, clinical, and functional data

- Demographic Data: Age and Sex.
- Psychiatric Comorbidities according to ICD-10: Schizophrenia, Schizotypal and Delusional Disorders (F20-F29); Mood Disorders (F30-F39); Neurotic, Stress-Related and Somatoform Disorders (F40-F48); Disorders of Adult Personality and Behaviour (F60-F69).
- Addictions: Alcohol and Tobacco dependence.
- COVID 19 symptoms: fever, cough, shortness of breath, muscle ache, headache, sore throat, rhinorrhea, chest pain, diarrhoea, nausea, and vomiting.
- The Charlson Comorbidity Score (CCS): is a comorbidity categorising tool issued from the Charlson Comorbidity Index and based on the International Classification of Diseases (ICD) (Charlson et al., 1994). Each comorbidity category has an associated weight (from 1 to 6), based on the adjusted risk of mortality or resource use. The sum of all the weights results in a single comorbidity score for each patient.
- The AGGIR Scale for Autonomie Gérontologie Groupes Iso-Ressources is a multidimensional tool that assesses the physical, mental, domestic, and social functioning of the elderly. It classifies them into homogenous groups ranging from GIR1, meaning dependant in all daily activities, to GIR 6, meaning autonomous (Coutton, 2001).
- Treatment was categorised in either: "Psychiatric medications" comprising antipsychotics, antidepressants, benzodiazepines, and mood stabilisers); or "Other categories, including antidiabetics, antihypertensives, anti-inflammatory, and miscellaneous.
- Laboratory findings were issued from real-time reverse transcriptase chain reaction test (RT-PCR): a sensitive (70%) and specific (100%) method to detect SARS CoV-2), carried out, according to French regulatory authorities recommendations, in residents clinically suspected of contracted infection(2020). On April 21st, 2020, all the residents underwent PCR and serology testing with lateral flow immunochromatography to detect SARS-CoV-2 antibodies in blood, serum, or plasma (Grzelak et al., 2020).

2.2.2. Diagnosis of COVID-19 and patient evolution

Diagnosis of COVID-19 was made on the following criteria

- COVID 19 laboratory-confirmed cases by positive RT-PCR results
- Patients who manifested acute respiratory distress with CT-Scan, revealing the characteristic images of ground glass, although the RT-PCR test was negative.
- Positive-serology testing in asymptomatic or paucisymptomatic patients during the study period.
- Covid symptom severity was categorised as follows asymptomatic, paucisymptomatic, symptomatic in need of hospitalisation, or requiring intensive care management
- Patient evolution: death or recovery. The survival period was measured in days from the onset of the disease (appearance of the first symptoms) until the end.

2.3. Statistics analysis

We used descriptive statistics to characterise each group of patients: the SMI and Non-SMI groups were compared for demographics and clinical parameters. Continuous measurements were expressed as mean and SD, and categorical variables as percentages (Tables 1 and 2 and Fig. 1).

Group differences were assessed with Chi2 statistics for categorical variables, student *t*-test for variables with normal distribution, and Kolmogorov-Smirnov for variables without normal distribution. In a first step, we conducted a univariate regression analysis to check the association between demographic, clinical, functional, and therapeutic variables (independent variables) and COVID-19 contamination (Yes/No) severe COVID-19 forms requiring hospitalisation (Yes/No), and Death (Yes/No) as dependant variables. Binary logistic regression models were built using only the independent variables that were significantly ($p < 0.05$) associated with the dependant variable. The variable Age has been added to the tested model. Survival analysis comparing time to death between the two groups was obtained on the Kaplan-Meier estimate

3. Results

3.1. Outbreak evolution

Amongst the 75 residents living in the facility on March 17th, 72 were included in the study. Three were excluded as they refused to participate. At the end of the study, we counted 58 Patients diagnosed with COVID-19 (15 with SMI and 43 without SMI); 31 were asymptomatic (10 with SMI); 27 were symptomatic. amongst the 27 symptomatic residents (5 with SMI and 22 without SMI), 14 required hospitalisations (2 with SMI and 12 without SMI), 13 were kept in the facility under strict medical monitoring. Three patients out of the 14

Table 1
compares demographic, clinical, functional, and therapeutic characteristics of the SMI group residents and their counterparts.

		SMI-R (24)	NON-SMI-R (48)	*p*
Age (SD)		71,8 (8.3)	84,5 (9,7)	0,00
Sexe F(%)		19 (79.2%)	32(66.7%)	0.27
Autonomy				
	AGGIR Score(SD)	2,71 (1,12)	2,38(1,24)	0,37
Comorbidities				
	Hypertension(%)	13 (54.2%)	32(66.7%)	0,3
	Diabetes(%)	10(41%)	7(14.6%)	0 ,01
	COPD(%)	4(16.7%)	5(10.4%)	0,45
	Dementia(%)	8(33%)	34(70%)	0,02
	Cancer(%)	4(8%)	1(4%)	0,51
CCI (SD)		5,13 (1,97)	3,17(1,43)	0,1
Smoking		5 (20.8%)	2 (4,16%)	0,02
Psychiatric treatments				
	Antipsychotics	21 (87.5%)	11(22.9)	0,00
	Benzodiazepines	17 (70.8%)	21(43.8%)	0.03
	Antidepressants	12(50%)	10(20.8%)	0.01
COVID-19				
	Incidence	15 (62.5%)	43(89.6%)	0,006
	SFRH (%COVID-19)	3 (20%)	12 (27.9%)	0,547
	Deceased(%COVID-19)	2(14,3%)	13(29.5%)	0.256

SMI-R: Residents with Severe Mental Illness; Non-SMI-R: Residents without severe mental illness; SD: Standard deviation; GIR: Score at the AGGIR scale (Autonomie Gérontologique Groupe Iso Ressources); COPD: Chronic obstructive pulmonary disease; CCI: Score at the Charlson comorbidity; COVID-19: Coronavirus disease 2019; SFRH: severe form requiring hospitalization.

who were hospitalised recovered. None of them suffered from SMI. In comparison, ten residents recovered in the non hospitalised group (3 with SMI and7 without SMI). Of the 14 patients who died from COVID19, 11 were hospitalised, and only two were suffering from SMI.

3.2. SMI and non-SMI groups comparison

The SMI group represented a third of the total participants; the mean age was 71.8 years (SD=8.3), and 79% were women. The non-SMI group was significantly older, with a mean age of 84.5 (SD=9.7); $p = 0.00$, with a similar gender distribution $p = 0,27$. Schizophrenia affected 22 SMI residents; one suffered from delusional disorder and another from bipolar disorder with psychotic features.

All participants with SMI were treated with antipsychotics, in most cases associated with other psychotropics (70% with benzodiazepines and 50% with antidepressants). Two of them received long-acting antipsychotics (Haldol decanoate, pipotiazine XR) and two were prescribed clozapine.

Prescription of psychotropics was also frequent in the non-SMI group; 11 residents (23%) were treated with antipsychotics mainly by low-dose risperidone, 21 (43.8%) received benzodiazepine, and 10 (20.8%) were under antidepressants. Autonomy level, measured by the AGGIR Scale, was comparable between the two groups (mean score of 2,71 [SD: 1,12] in the SMI arm and 2,38 [SD: 1.24] in the non-SMI; $p = 0.37$).

The Charlson Comorbidity score was not significantly different across the two groups (CCI mean score 3.17 [SD=1.43] in the SMI group versus 5.13 [ET=1.97] in the non-SMI arm). Comorbid entities were, however, unevenly distributed between the two groups. Diabetes was significantly more prevalent in the SMI group($p = 0.01$), and neurodegenerative diseases were significantly more frequent in the non-SMI ($p = 0.02$).

Tobacco use was significantly more prevalent in the SMI group (20.8% versus only two residents, 4% in the non-SMI group).

During the study period, COVID 19 incidence was significantly higher in the non-SMI group 89% versus 62% in the SMI one; $p = 0.006$. Symptomatic forms were not significantly more prevalent in the SMI group (51% vs 33%; $p = 0,23$) neither rate of hospitalization (27,9% vs 20%; $p = 0,547$) nor mortality (27,9% vs 13,3%; $p = 0, 25$).

3.3. Univariate and multivariate regression analysis

Univariate logistic regression shows two variables as significantly associated with a lower incidence of COVID-19: autonomy as measured by the AGGIR scale (OR=0.57; $p = 0.03$; 95%CI [0.34–0.94]) and psychiatric status (OR=0.19; $p = 0.01$; 95%CI [0.05–0.67]). Both variables were then selected to built a multivariate logistic regression model. Autonomy (OR=0.56; $p = 0.044$; 95%CI [0.32–0.98]) as well as psychiatric status (OR=0.19; $p = 0.01$; 95%CI [0.05–0.72] remained significantly associated with a lower COVID-19 incidence.

The female gender ($p = 0.03$) and antidepressant treatment ($p = 0.04$) stand out in univariate regression analysis as significantly associated with less severe COVID-19 forms. In a multivariate logistic regression model combining both variables with age, considered a significant predictive factor of SFRH, only antidepressant treatment remained significantly associated with less severe forms (OR=0.1; $p = 0.04$; 95%CI[0.01–0.99]).

Survival duration between disease onset and death did not significantly differ between the two groups, with a median time of 8 days in SMI-R and 15 days in Non-SMI-R ($p = 0,91$).

4. Discussion

In our study, residents suffering from SMI had a lower incidence of COVID-19 than residents without SMI. Once contracted, however, the two groups did not significantly differ concerning disease severity and mortality. As expected, better autonomy was associated with lower COVID-19 infection. Lower levels of self-sufficiency require sustained staff assistance, thus further exposure to infection, as the virus can not be transmitted by means other than staff personnel in lockdown conditions. Although considerably older, residents without SMI did not differ in autonomy score from their SMI suffering counterparts who required staff assistance at a comparable level. Thus, the two groups could be considered at equal risk of being infected. In line with the literature, the female gender is associated, in our study, with a reduced risk of SFRH (Di Stadio et al., 2020). Patients receiving antidepressants had a significantly lower risk to develop severe COVID-19 forms. When combined with gender and age, antidepressant treatment remained significantly associated with a reduced risk of SFRH. This result corroborates previous data from the literature suggesting a potential preventive role of antidepressants toward severe forms of the disease (Stingl, 2021).

Epidemiological data collected in France suggested a lower incidence of COVID-19 in psychiatric patients compared to healthcare staff. Similar observations have been reported in psychiatric wards in China, Spain, and Italy (Plaze et al., 2020).

Amongst explanatory hypotheses, some authors suggested a potential antipsychotic preventive action towards SARS-CoV2. This hypothesis is consistent with the already known antiviral properties (against the influenza virus, HIV, hepatitis C) of several antipsychotics commonly used in psychiatry (Villoutreix et al., 2020), particularly chlorpromazine (Plaze et al., 2020).

In our study, all residents with SMI received at least one antipsychotic. The lower disease incidence in the SMI group could be related to a possible antipsychotic protective action. Nonetheless, eleven (24%) non-SMI residents under antipsychotic therapy were contaminated. To our knowledge, ongoing research on chlorpromazine repurposing in

Table 2
Univariate and multivariate analysis for COVID-19 contamination and severe forms requiring hospitalisation.

	COVID-19 Yes 58	No 14	Univariate p-value	Multivariate Logistic p-value	Odds ratio [95% CI]	SFRH Yes 15	No 43	Univariate p-value	Multivariate Logistic p-value	Odds ratio [95% CI]
Age (SD)	81.2 (10.7)	79 (13,58)	0.18			77.67 (8.9)	82.5(11)	0.2	0.14	0.95[0.88-1.01]
Gender(F)(%)	43 (59.7%)	8 (11.1%)	0.21			8(11.1%)	35 (48.61%)	0.03	0.05	0.25[0.06-1.03]
AGGIR Score(SD)	2.3(1.1)	3.1(1.1)	0,02	0.03	0.55[0.34-0.94]	2.53 (1.45)	2.26 (1.07)	0.53		
CCI(SD)	4.5(2)	4.1(1.9)	0.49			5.13(2.2)	4.35(1.9)	0.61		
Comorbidities										
HT	37 (51.4%)	8 (11.1%)	0.64			7(9.72%)	30 (41.67%)	0.1		
Diabetes	14 (19.4%)	3(4.2%)	0.83			1(1.38%)	13 (18.05%)	0.06		
COPD	8 (11.1%)	1(1.4%)	0.5			3(4.16%)	5(6.94%)	0.42		
Dementia	36(50%)	6(8.3%)	0.19			11 (15.27%)	25 (34.72%)	0.3		
Cancer	4(5.6%)	1(1.4%)	0.97			3(4.16%)	1(1.38%)	0.05		
SMI	15 (20.8%)	9 (12.5%)	0.01	0.01	0.19[0.05-0.67]	3(4.16%)	12 (16.6%)	0.54		
Smoker	4(5.6%)	3(4.2%)	0.17			1(1.38%)	3(4.16%)	0.96		
Psychiatric Treatments										
Antipsychotic	25 (34.7%)	7(9.7%)	0.64			7(9.72%)	18(25%)	0.74		
Benzodiazepine	30 (41.7%)	8 (11.1%)	0.71			7(9.72%)	23 (31.94%)	0.64		
Antidepressant	15 (20.8%)	7(9.7%)	0.08			1(1.38%)	14 (19.4%)	0.04	0.04	0.1[0.01-0.99]

95% CI: Confidence interval at 95%; AGGIR: Score at the AGGIR scale (Autonomie Gérontologique Groupe Iso Ressources); CCI: Score at the Charlson comorbidity index; COPD: Chronic obstructive pulmonary disease; COVID-19: Coronavirus disease 2019; HT: Hypertension; SD: Standard deviation; SFRH: Severe Form Requiring Hospitalization; SMI Severe Mental Illness.

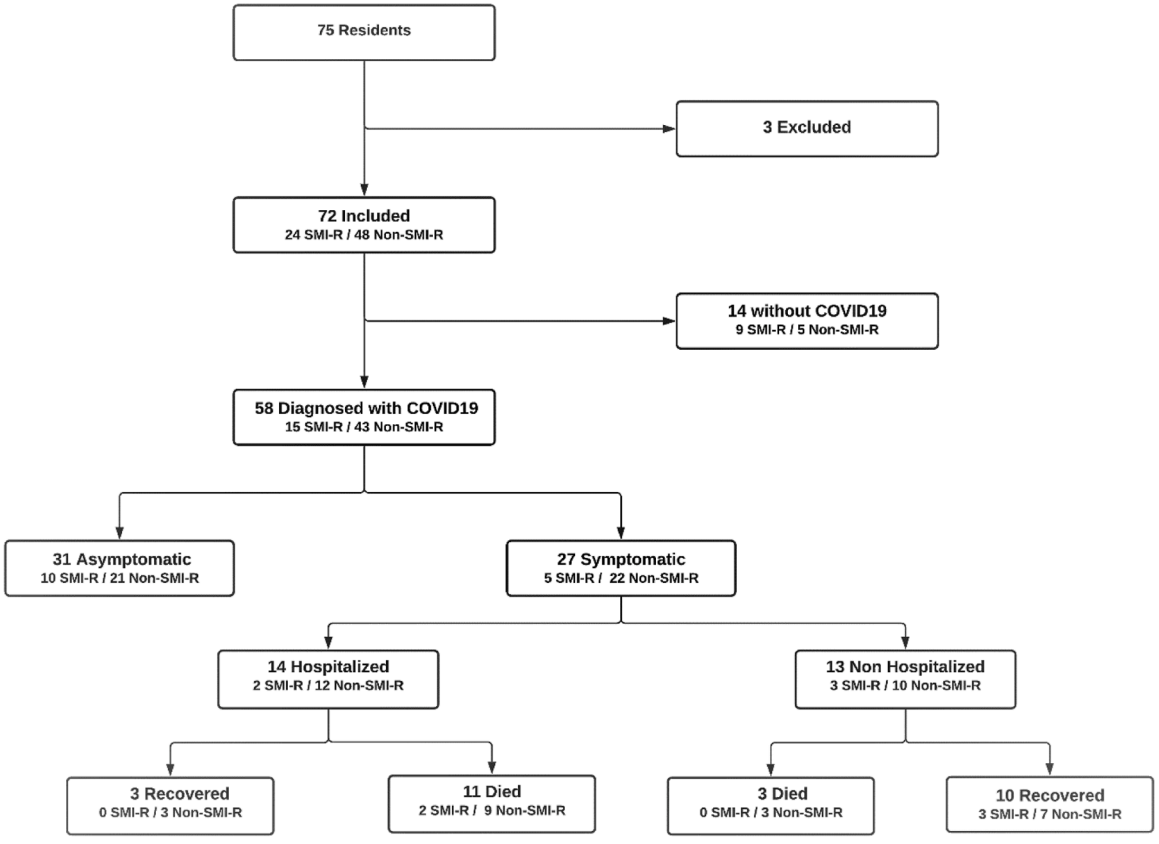

Fig. 1. Outbreak Evolution amongst Residents Between March 17th and May 11th 2021.

COVID19 treatment did not yet lead to any conclusive results. Further, no association was found between chlorpromazine or haloperidol prescription and reduced morbimortality from COVID19 (Hoertel et al., 2021b; Hoertel et al., 2021c).

A growing body of research suggests that antidepressants and, to a lesser extent, antipsychotics may prevent the infection of epithelial cells with SARS-CoV-2 through functional inhibition of acid sphingomyelinase or FIASMA (Kornhuber et al., 2021). Further, an observational cohort study reported a significant association between SSRI and non-SSRI antidepressant use and reduced risk of intubation or death in COVID19 patients (Hoertel et al., 2021a). In our study, patients treated with antidepressant drugs are at lower risk to contract COVID-19 on the one hand and significantly less prone to develop SFRH on the second hand. Hence, our results support the hypothesis of an antidepressant preventive effect on COVID-19 deterioration.

Smoking, a widespread addiction in patients with severe psychiatric disorders (Dervaux and Laqueille, 2008), has been associated with a decreased probability of testing positive for SARS CoV2 infection (Rentsch et al., 2020). In vivo models support a potential protector effect of nicotine against SARS-CoV2 cell entry via a possible role of nicotinic acetylcholine receptors (Oliveira et al., 2020). Our study did not find a significant association between smoking and a lower infection rate. However, no firm conclusions can be drawn due to our sample's small proportion of smokers.

Many authors have raised the hypothesis of pre-existing immunity to SARS CoV2 to explain the variability of the disease's incidence and severity across populations (Severance et al., 2011).

Prenatal influenza exposure confers an increased risk of psychosis (Brown et al., 2004). Like influenza viruses, human coronaviruses are neurotropic (Beraki et al., 2005). They can enter the brain via the olfactory neural pathway, causing brain damage, producing psychotic disorders (Netland et al., 2008). Clinical reports of psychotic symptoms such as auditory hallucinations have been described in coronavirus infection studies (Cheng et al., 2004). Thus coronaviruses are considered good candidates for schizophrenia aetiological research. All the more so, serological studies reported higher immunoreactivity for certain coronavirus strains in individuals with schizophrenia spectrum disorders than controls without a history of psychiatric disease (Severance et al., 2011). The hypothesis of a protective cross-immunity in SMI residents, although very unlikely, can not be ruled out until extensive immunological explorations.

Despite better knowledge of psychiatric pathology, mental health professionals observe the same social distancing toward patients with a psychiatric disorder, particularly schizophrenia, as the general population (Nordt et al., 2006). Medico social staff is no exception to this disposition (Grabowski et al., 2010; Rahman et al., 2013). Patients with schizophrenia have marked difficulties engaging and maintaining community life and group activities (Green et al., 2018). Physical distancing is all the more significant as the pathology is active in a paranoid mode (Schoretsanitis et al., 2016). The addition of the distance to patients due to stigmatisation to distance resulting from pathological withdrawal could result in a physical distancing toward potential virus transmitters, preventing SMI suffering residents from contracting the disease.

Although our limited sample size prevents us from firmly concluding, our results challenge the idea that SMI residents are more prone to contracting the disease and require more restrictive confinement measures during pandemics than non-SMI residents.

Further studies in a larger population with a more accurate clinical characterisation of residents and evaluating the quality of care are needed to ascertain the results and better understand the potential differences of SARS CoV2 spreading according to psychiatric status

Author statement

All the authors contributed equally to this work.

Conflict of Interest Statement

The Authors declare No conflict of Interest

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