

# COVID-19 Prevalence and Mortality Among Schizophrenia Patients: A Large-Scale Retrospective Cohort Study

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**Objective:** Individuals with schizophrenia may be at an increased risk for COVID-19 morbidity due to the disease characteristics. In this study, we aimed to explore the odds of significant COVID-19 morbidity and mortality among schizophrenia patients while controlling for potential sociodemographic and medical confounders. **Methods:** Schizophrenia patients and age-and-sex matched controls (total  $n = 51\,078$ ) were assessed for frequency of COVID-19 positivity, hospitalizations, and mortality. The odds for COVID-19-associated hospitalization and mortality were calculated using logistic regression models, while controlling for age, sex, marital status, sector, socioeconomic status, diabetes, ischemic heart disease, hypertension, hyperlipidemia, obesity, smoking, and chronic obstructive pulmonary disease. **Results:** Individuals with schizophrenia were less likely to test positive for COVID-19; however, they were twice as likely to be hospitalized for COVID-19 (OR 2.15 95% CI 1.63–2.82,  $P < .0001$ ), even after controlling for sociodemographic and clinical risk factors (OR 1.88 95% CI 1.39–2.55,  $P < .0001$ ). Furthermore, they were 3 times more likely to experience COVID-19 mortality (OR 3.27 95% CI 1.39–7.68,  $P < .0001$ ), compared to controls. **Conclusions:** We found evidence of associations between schizophrenia and increased COVID-19 morbidity and mortality compared to controls regardless of sociodemographic and medical factors. As these patients present with a combination of potential risk factors for mortality, efforts should be made to minimize the effects of the pandemic on this vulnerable population.

**Key words:** schizophrenia/COVID-19/cohort/mortality/hospitalization

## Introduction

The social, economic, and health-related consequences of the novel coronavirus (COVID-19) pandemic, caused by the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have been documented extensively. Studies exploring the consequences of the pandemic have demonstrated its effects on the general population,<sup>1,2</sup> as well as on at-risk groups such as individuals with racial, ethnic, and income disparities.<sup>3</sup> Nonetheless, the effect of the pandemic on vulnerable groups such as individuals with severe mental illness has not been fully delineated thus far. Kozloff et al<sup>4</sup> recently suggested that individuals with schizophrenia may be considered an at-risk group, as some clinical (ie, cognitive impairment and poor insight) and sociodemographic (ie, living in congregate housing) characteristics may increase the risk of infection among this population. Furthermore, they suggested that these patients may be more prone to premature death due to their poor physical health. Indeed, many studies have demonstrated that individuals with schizophrenia and other severe mental illnesses have an excess of physical comorbidities and consequent reduced life expectancy,<sup>5,6</sup> as well as a higher prevalence of deaths from pneumonia and influenza.<sup>7</sup> Nonetheless, only a few studies have systematically evaluated whether schizophrenia patients are indeed at risk for either infection or premature death due to COVID-19.

Empirical studies examining the association between psychiatric disorders and COVID-19 infections and complications have only recently begun to emerge. Merzon et al<sup>8</sup> suggested that patients with attention-deficit/hyperactivity disorder (ADHD) may be more prone to become

infected with COVID-19 due to their limited ability to comply with COVID-19 prevention recommendations. They assessed the prevalence of ADHD patients among 14,022 cases of COVID-19 positive patients and found significantly higher rates of ADHD patients in this population. Reilev et al<sup>9</sup> performed a population-based study to assess factors that might contribute to a higher risk of severe and fatal COVID-19 disease among Danish individuals, and found that a major psychiatric disorder increased the odds of mortality by 2.4–2.7. To the best of our knowledge, only one study has assessed the association between schizophrenia diagnosis and severity of COVID-19 illness: Fond et al<sup>10</sup> performed a case-control study of 1092 patients admitted to acute care hospitals due to COVID-19 illness in Marseille, France, and found increased mortality rates among patients with schizophrenia (26.7%) compared to patients without schizophrenia (8.7%). Nonetheless, the authors stated that the sample of schizophrenia patients included only 15 cases, and the database suffered from missing data and potential inaccuracies, precluding strong conclusions.<sup>10</sup> Thus, the association between schizophrenia and prevalence of infections, as well as with severity of illness, remains to be examined.

In this study, we aimed to bridge the gap in the epidemiological literature related to the prevalence of COVID-19 morbidity and mortality among individuals with schizophrenia. Specifically, we aimed to address the following empirical research questions: (1) Are patients with schizophrenia more prone to COVID-19 infections? (2) Do patients with schizophrenia have a more severe course of COVID-19 illness, as manifested by higher rates of hospitalization and mortality? To address these research questions, we updated a validated database of schizophrenia patients and their age-and-sex matched controls (total  $n = 51\,078$ ) with recent data pertaining to the current epidemic. COVID-19 data included number of COVID-19 tests, COVID-19 hospitalizations, and COVID-19 mortality rates. Sociodemographic and medical risk factors were entered as covariates and included age, sex, marital status, sector, socioeconomic status, obesity, smoking, diabetes, hyperlipidemia, chronic obstructive pulmonary disease (COPD), and ischemic heart disease (IHD). Based on the reviewed literature, we hypothesized that schizophrenia patients would show higher positive results, as well as higher rates of hospitalization and mortality.

## Methods

### Data Source

The study utilized the databases of the Clalit Health Organization (CHS), the largest operating healthcare organization in Israel.<sup>11</sup> The CHS is 1 of 4 operating healthcare organizations to provide healthcare for all citizens of Israel and covers nearly 5 million citizens, over 50% of the country's population,<sup>12</sup> through 1427 primary

healthcare units and additional medical facilities. Clalit Health Services regularly updates its databases with real-time information derived from medical care facilities and hospitals, pharmacies, and administrative medical operating systems. The data mining of the current database was based on the registries of the CHS, which undergo periodic validation processes such as direct comparisons between various diagnostic sources and random evaluations of medical files. Diagnoses and medical fields were obtained through the chronic diseases registry, which has been previously validated by the developers of its algorithms,<sup>13</sup> as well as by many other authors utilizing the database.<sup>14–17</sup> The establishment of the computerized systems was initiated in 2000 and is continuously updated with clinical information. The extraction of the current database, containing schizophrenia patients and their matched controlled cases, was originally mined at the end of 2017.<sup>18</sup> Since the beginning of the pandemic, patients have been able to be tested for COVID-19 through their primary care clinics, in mass drive-in facilities initiated by the Ministry of Health and local city municipalities, through first-aid mobile staffs, and in general and psychiatric hospitals. COVID-19 information is automatically synchronized with the CHS, the Ministry of Health, and primary care databases through the registered, licensed laboratories in Israel authorized to analyze polymerase chain reaction (PCR) panels from all sources performing the tests. For the purposes of the current study, the database was updated for COVID-19 and demographic fields in October 2020. This update included mortality rates; therefore, individuals who were deceased prior to the onset of the pandemic were removed from the database along with their matched controls.

### Definition of Study Variables

Diagnosis of schizophrenia was based on a community senior psychiatrist's medical registration or if listed on a psychiatric hospital's discharge letter. To qualify for a schizophrenia diagnosis, the file had to contain one of the ICD-9 codes for schizophrenia (code 295) or one of the ICD-10 codes for schizophrenia (code F20).<sup>19,20</sup> Validation of accuracy of schizophrenia diagnosis had been previously performed by an expert senior psychiatrist who reviewed the clinical files of 10% of the sample and found a 94% accuracy rate.<sup>18</sup> Control group participants comprised random cases from the population of CHS-insured citizens, which were matched by age and gender to the schizophrenia group. These included individuals with no diagnosis of schizophrenia who were insured by the CHS at the time of data mining and randomly sampled at a 1:1 ratio. Age was matched with a maximum allowable difference of 1 year, and sex was matched at a 1:1 ratio.

COVID-19 characteristics included results of COVID-19 tests, number of tests taken, hospitalizations, and

deaths. In Israel, multiple diagnostic polymerase chain reaction (rRT-PCR) panels, which were approved by the Ministry of Health, are utilized, such as Xpert Xpress SARS-CoV-2 (Cepheid) and the real-time fluorescent RT-PCR kit for detecting 2019-nCoV (BGI Genomics). Test results were available and retrieved from March 2020 to October 2020. Referrals for PCR tests were initially given if patients reported COVID-19 symptoms or were in close contact with COVID-19 positive patients. After the first lockdown in April 2020, alongside the expansion of the national capacity to perform PCR testing for COVID-19, indications for testing were expanded and included early testing of asymptomatic direct contacts of COVID cases, periodic screening of health workers working with vulnerable populations, screening of patients before elective surgery, and screening of patients before admission for long-term psychiatric hospitalization. Hospitalization data were reported by general hospitals to the Ministry of Health and synchronized with the CHS databases, and death reports were derived from hospital discharge letters and were also verified by cross-examination with the Interior Ministry databases.

The following clinical conditions were examined as potential risk factors for COVID-19 hospitalization and death: smoking (ICD-9 code 3051, V1582), which refers to a chronic diagnosis as registered by a community physician or as listed in the diagnoses of discharge letters, obesity (ICD-9 codes 278, 75981), diabetes (ICD-9 codes 250, 3620), hypertension (ICD-9 codes 401–405), hyperlipidemia (ICD-9 codes 2720), chronic obstructive pulmonary disease (COPD, ICD-9 codes of 4912, 4920, 4928, 496 and 515) and ischemic heart disease (IHD, ICD-9 codes of 410–414, 429, V458, Z360–Z261). ICD codes were also verified using textual identification and lab test results. Socioeconomic status was obtained using the CHS index, calculated as an index score combining information from social services, as well as sociodemographic variables such as district and current address. Sector was used to denote the main subpopulations in Israel (general, Ultraorthodox, and Arab). The study was reviewed and approved by the CHS institutional review board (IRB), where informed consent was waived due to the nature of data extraction.

### Statistical Analysis

Differences in prevalence of sociodemographic characteristics, medical conditions, and COVID-19 parameters between the schizophrenia and control group were examined using univariate logistic regressions for categorical variables and t-tests for continuous variables. Univariate and multivariate logistic regressions were employed to examine the odds for COVID-19 testing, COVID-19 positive cases, and COVID-19 hospitalization and mortality, among individuals with schizophrenia compared to controls, while reporting the base-adjusted model

(adjusted for age and sex), the model accounting for sociodemographic and socioeconomic factors (marital status, sector, and socioeconomic status), and the model accounting for clinical risk factors (obesity, smoking, diabetes, hyperlipidemia, COPD, and IHD). Odds ratios and 95% confidence intervals were reported, as well as significance levels as set to 5%. All statistical analysis was performed using SPSS software, version 25 (SPSS).

### Results

**Table 1** presents the sociodemographic and clinical characteristics of the study participants. Participants were 25 539 individuals with schizophrenia and their age- and-sex matched controls. Mean age was 51.51 among individuals with schizophrenia (SE = 15.42) and 51.37 among controls (SE = 15.70). A total of 15 572 men (61.0%) were sampled in both groups. Compared to age- and-sex matched controls, individuals with schizophrenia were significantly less likely to be married [OR 0.19 95% CI 0.18–0.2] and to belong to the Ultraorthodox sector [OR 0.61, 95% CI 0.58–0.64], and were more likely to present with a low [OR 1.88, 95% CI 1.79–1.98] or medium [OR 1.80, 95% CI 1.71–1.89] socioeconomic status. Examination of clinical characteristics indicated that individuals with schizophrenia were significantly more likely to receive a lifetime diagnosis of obesity [OR 1.68 95% CI 1.61–1.75], smoking [OR 1.64 95% CI 1.59–1.70], diabetes [OR 1.65 95% CI 1.58–1.73], hyperlipidemia [OR 1.44 95% CI 1.39–1.49] or COPD [OR 2.32 95% CI 2.09–2.76], and significantly less likely to receive a diagnosis of IHD [OR 0.67 95% CI 0.64–0.74]. As can be expected, psychiatric admissions were more prevalent in schizophrenia patients compared to the controls, with prevalence of 1.4% compared to 0.0% in the controls [OR 91.78 95% CI 34.25–245.91].

**Table 2** presents the COVID-19 disease characteristics among schizophrenia and control participants. Of the entire sample (total  $n = 51\,078$ ), 13 350 (26.2%) individuals were tested for COVID-19, and 1358 (2.6%) screened positive for COVID-19. In addition, 238 (0.5%) were hospitalized, out of whom 29 died (12.2%). Within the schizophrenia patient group, 642 patients tested positive, 162 (25.23% of those who tested positive) were hospitalized for COVID-19, and 22 (3.42% of those who tested positive) died due to COVID-19. Of the control group, 709 patients tested positive, 76 (10.71% of those who tested positive) were hospitalized for COVID-19, and 7 (0.9% of those who tested positive) died due to COVID-19. Univariate comparative analyses indicated that individuals with schizophrenia were significantly more likely to be tested for COVID-19 [OR 1.52 95%CI 1.46–1.58] and underwent more tests compared to controls [OR 1.19 95%CI 1.17–1.21]. They were also significantly less likely to receive a positive diagnosis of COVID-19 compared to controls [OR 0.64 95%CI 0.57–0.71]. Nonetheless,

**Table 1.** Prevalence of Sociodemographic Variables and Previously Diagnosed Background Medical Conditions Among the Study Population, Comparing Individuals With a Diagnosis of Schizophrenia to a Matched Sample of Controls

	Schizophrenia ( <i>n</i> = 25 539)	Control ( <i>n</i> = 25 539)	Odds Ratio	<i>P</i> -value
	<i>n</i> (%)	<i>n</i> (%)	OR [95% CI]	
Age ( <i>M</i> , <i>SD</i> )	51.51 (15.42)	51.37 (15.70)	N/A	N/A
Sex (% male)	15 572 (61.0)	15 572 (61.0)	N/A	N/A
Socioeconomic status (high)				
Low	11 937 (46.7)	10 536 (41.3)	1.88 [1.79–1.98]	<.0001
Medium	10 140 (39.7)	9397 (36.8)	1.80 [1.71–1.89]	<.0001
Sector				
Arab (general)	5855 (22.9)	3891 (15.2)	1.36 [1.25–1.47]	<.0001
Ultraorthodox (general)	1047 (4.1)	1540 (6.0)	0.61 [0.58–0.64]	<.0001
Marital status (married)	5462 (21.4)	15 123 (59.2)	0.19 [0.18–0.2]	<.0001
Smoking <sup>b</sup>	13 175 (51.6)	10 033 (39.3)	1.64 [1.59–1.70]	<.0001
Obesity	8295 (32.5)	5691 (22.3)	1.68 [1.61–1.75]	<.0001
Diabetes	5279 (20.7)	3476 (13.6)	1.65 [1.58–1.73]	<.0001
Hypertension	5123 (20.1)	5138 (20.1)	1.00 [0.95–1.04]	.868
Hyperlipidemia	12 120 (47.5)	9828 (38.5)	1.44 [1.39–1.49]	<.0001
COPD	1172 (4.6)	519 (2.0)	2.32 [2.09–2.76]	<.0001
IHD	1171 (4.6)	1667 (6.5)	0.67 [0.64–0.74]	<.0001
Psychiatric admissions	362 (1.4)	4 (0.0)	91.78 [34.25–245.91]	<.0001

Note: OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; IHD, ischemic heart disease.

<sup>a</sup>Reference group in parentheses.

<sup>b</sup>Reference group is not having the condition.

**Table 2.** COVID-19 Morbidity Characteristics and Mortality Rates, Comparing Individuals With a Diagnosis of Schizophrenia to a Matched Sample of Controls

	Schizophrenia ( <i>n</i> = 25 539)	Control ( <i>n</i> = 25 539)	OR (95% CI)	<i>P</i>
Tested for COVID-19 ( <i>n</i> , % tested)	7708 (30.2%)	5642 (22.1%)	1.52 (1.46–1.58)	<.0001
Mean number of tests per participant ( <i>M</i> , <i>SD</i> )	3.82 (4.13)	2.13 (2.78)	1.19 (1.17–1.21)	<.0001
Positive for COVID-19 ( <i>n</i> , %)	649 (2.5%)	709 (2.8%)	0.64 (0.57–0.71)	<.0001
Hospitalized due to COVID-19 ( <i>n</i> , %)	162 (0.6%)	76 (0.3%)	2.13 (1.62–2.81)	<.0001
Death due to COVID-19 ( <i>n</i> , %)	22 (0.1%)	7 (0.0%)	3.14 (1.34–7.36)	<.0001

Note: OR, odds ratio; CI, confidence interval.

individuals with schizophrenia were more than twice as likely to be hospitalized due to COVID-19 [OR 2.13 95%CI 1.62–2.81 *P* < .0001] and more than 3 times more susceptible to COVID-19 mortality [OR 3.14 95%CI 1.34–7.36 *P* < .0001], compared to controls.

Table 3 presents the odds of COVID-19 morbidity and mortality among individuals with schizophrenia and their matched controls while adjusting for sociodemographic and clinical factors. As can be viewed, the odds for COVID-19 hospitalization among schizophrenia patients remained significant after controlling for sociodemographic factors [adjusted odds ratio (AOR) 1.85 95%CI 1.37–2.50] and for clinical factors [AOR 1.88 95%CI 1.39–2.55]. For mortality, the base-adjusted model (controlling for age and sex) indicated that schizophrenia patients were more than 3 times more likely to experience COVID-19 mortality [AOR 3.27 95%CI 1.39–7.68]. Exploratory analyses controlling for additional covariates indicated that this association also remained

after controlling for sociodemographic [AOR 2.79 95%CI 1.16–6.72] and clinical factors [AOR 2.77 95%CI 1.13–6.79]; nonetheless, due to the low number of overall deaths, these models should be interpreted with caution.

An exploratory analysis examining the characteristics of hospitalized and deceased individuals indicated that hospitalized schizophrenia patients were predominantly males at a higher mean age and with a higher prevalence of smoking, obesity, diabetes, and COPD. When examining mortality from COVID-19, deceased individuals with schizophrenia were at a lower mean age, as well as there being a higher proportion of men, smoking, and COPD. These rates were not comparable due to low sample size (Table 4).

### Discussion

In this study, we assessed the odds for hospitalization and mortality due to COVID-19 in a large sample of individuals

**Table 3.** Odds ratio and 95% Confidence Interval of COVID-19 Hospitalizations and Mortality Among Schizophrenia Patients Compared to Matched Control Participants, Controlling for Demographic and Clinical Characteristics

	Control (n = 25 539)	Schizophrenia (n = 25 539)	P-value	Low 95%	High 95%
	OR	OR			
Hospitalization					
Model 1 <sup>a</sup>	1	2.15	<.0001	1.63	2.82
Model 2 <sup>b</sup>	1	1.85	<.0001	1.37	2.50
Model 3 <sup>c</sup>	1	1.88	<.0001	1.39	2.55
Mortality					
Model 1 <sup>a</sup>	1	3.27	<.01	1.39	7.68

Note: OR, odds ratio.

<sup>a</sup>Base-adjusted model (adjustment for age and sex).

<sup>b</sup>Additional adjustment for marital status, sector, and socioeconomic status.

<sup>c</sup>Additional adjustment for smoking, obesity, diabetes, hyperlipidemia, hypertension, chronic obstructive pulmonary disease (COPD), and ischemic heart disease (IHD).

**Table 4.** Descriptive Characteristics of Hospitalized and Deceased Individuals Among Schizophrenia Patients and Controls

	Hospitalized		Deceased	
	Control (n = 76)	Schizophrenia (n = 162)	Control (n = 7)	Schizophrenia (n = 22)
Mean age (SD)	57.07 (16.10)	59.94 (15.83)	75.14 (9.75)	71.64 (11.47)
Sex = men	42 (55.3%)	88 (54.3%)	2 (28.6%)	8 (36.4%)
Smoking	23 (30.3%)	64 (39.5%)	0 (0.0%)	11 (50.0%)
Obesity	25 (32.9%)	68 (42.0%)	4 (57.1%)	7 (31.8%)
Diabetes	23 (30.3%)	55 (34.0%)	4 (57.1%)	9 (40.9%)
Hypertension	30 (39.5%)	62 (38.3%)	6 (85.7%)	12 (54.5%)
Hyperlipidemia	47 (61.8%)	92 (56.8%)	6 (85.7%)	16 (72.7%)
COPD	2 (2.6%)	19 (11.7%)	0 (0%)	6 (27.3%)
IHD	13 (17.1%)	19 (11.7%)	2 (28.6%)	6 (27.3%)

Note: COPD, chronic obstructive pulmonary disease; IHD, ischemic heart disease.

with schizophrenia and an age-and-sex matched group of controls. The results of the analyses indicated that individuals with schizophrenia were significantly more likely to be tested for COVID-19 and less likely to receive a positive diagnosis of COVID-19. Nonetheless, they were twice as likely to be hospitalized due to the disease and 3 times more likely for COVID-19 mortality compared to controls. These associations were sustained even after adjusting for marital status, sector, socioeconomic status, smoking, obesity, diabetes, hyperlipidemia, COPD, and IHD.

Contrary to our initial hypothesis, individuals with schizophrenia were tested more frequently, and were less likely to test positive for COVID-19. These results also contradict previous predictions, which foresaw higher rates of infection within this population.<sup>4,21,22</sup> Furthermore, in a recent case-control study conducted in the United States,<sup>23</sup> the authors reported significantly higher odds (9.89) of COVID-19 infection among recently diagnosed schizophrenia patients (within the past year), with lower odds (1.48) in patients with a lifetime diagnosis of schizophrenia. One potential explanation to account for these differences in rates of infection may

be related to the medical policies employed by the Israeli Ministry of Health. The fact that patients with schizophrenia were tested more frequently than the controls may be associated with the mandatory testing policy implemented in psychiatric institutes and outpatient clinics in Israel, which require patients to be tested prior to hospital admission and/or psychiatric care. This policy of early COVID-19 detection may also have been applied in sheltered community homes and supervised rehabilitation centers, and may account for the lower prevalence in positive cases among the schizophrenia group. Future studies should explore whether facilities with such mandatory policy have differential infection rates, and whether inpatients and outpatients differ in odds for infection and morbidity. Another potential explanatory mechanism to account for the lower rates of infection is that social isolation, as well as the fact that the majority of individuals with schizophrenia were unmarried and less likely to have been infected by family members (which are considered to be one of the main routes of infection<sup>24,25</sup>), may resulted in reduced chances of infection. Such competing hypotheses should be subjected to future research.

Despite being tested more and having lower infection rates, our findings indicate that individuals with schizophrenia are significantly more likely to require intensive medical care, as reflected by the higher rates of hospitalization. These findings correspond to those reported by Wang et al,<sup>23</sup> who found higher rates of COVID-19 hospitalizations among patients with severe mental illnesses in the United States. It has been previously offered that biological factors related to neuroinflammation may contribute to the association between psychiatric disturbances and COVID-19,<sup>26</sup> mainly in patients with a new onset of psychiatric symptoms. An additional explanation to account for the higher rates of hospitalization is related to medical, behavioral, and environmental risk factors. Schizophrenia patients are more likely to suffer from comorbid medical conditions<sup>27</sup> and suffer from social isolation, which may interfere with early help-seeking behavior.<sup>28</sup> As a consequence, they may present themselves for medical care only when their condition has already worsened. This, as well as lower access to knowledge and lack of access to quality preventative services,<sup>29</sup> might explain the more severe trajectory of illness exhibited by these patients. Such potential pathways should be subjected to future research.

The higher COVID-19 mortality rates detected among schizophrenia patients align with previous predictions regarding the potential adverse consequences of high physical comorbidity among these patients.<sup>4</sup> Schizophrenia patients were more likely to be diagnosed with obesity, smoking, diabetes, hyperlipidemia, and COPD, and significantly less likely to receive a diagnosis of IHD. These findings correspond with previous reports.<sup>16</sup> Previous studies have also demonstrated a pattern of higher IHD mortality, yet lower or no increased risk of IHD in schizophrenia,<sup>16,30</sup> a finding that has been suggested to be associated with lower help-seeking behavior.<sup>31–33</sup> The higher rates of mortality also confirm the results reported by Fond et al,<sup>10</sup> who found a significantly higher prevalence of schizophrenia diagnoses among individuals admitted to acute care hospitals in France. Previous studies have indicated that aside from baseline physical comorbid illnesses, schizophrenia patients engage in smoking behavior more frequently and are therefore more vulnerable to smoking-related illnesses such as COPD,<sup>16</sup> which is considered a risk factor for COVID-19 mortality. These results highlight the convergence of several prominent risk factors for COVID-19 mortality among schizophrenia patients, as well as the need to address modifiable risk factors via adequate preventative interventions.

The findings of this study have several important clinical and empirical implications. Although the findings indicate a higher mortality risk among schizophrenia patients, the absolute number of deaths (22 in the schizophrenia group, 7 in the controls) and hospitalizations (162 in the schizophrenia group and 72 in the controls) was low. As the odds of significant COVID-19 morbidity

and mortality among schizophrenia patients were high even after adjusting for clinical factors, future studies should further explore additional explanatory routes that might lead to detrimental outcomes among this population. Such routes may be associated with potential medications and side effects,<sup>34</sup> factors contributing to illness management, and factors related to quality healthcare. Clinically, the results of the study stress the need to focus intervention efforts on modifiable factors that might minimize mortality rates among these patients.

Several limitations should be noted. The study population comprised patients with a schizophrenia diagnosis and cases which were matched by age and sex. Thus, the sample utilized in this study is not a representative sample. The present study focused on the presence of associations between schizophrenia and COVID-19 morbidity and mortality, and therefore no conclusive inferences can be made regarding causality. Although this is a large-scale study, the relatively small number of deceased individuals does not allow for sufficient statistical power to characterize specific factors associated with mortality among individuals with schizophrenia, and further studies are needed in order to allow for statistical inference of these effects. The CHS registry does not contain information about severity of schizophrenia; therefore, the pattern of associations between COVID-19 morbidity and mortality across different severity levels should be subjected to future research. The database utilized in this study was mined in 2017; therefore, individuals who were diagnosed with schizophrenia within the last 3 years were not included in this analysis. Future studies can determine whether the results reported in this study replicate across patients with a recent schizophrenia diagnosis. Finally, our study did not address the number of comorbid medical conditions presented by patients, which may be an additional risk factor for hospitalization and mortality.<sup>35</sup> Despite these limitations, the results of the current study clearly indicate that individuals with schizophrenia are a population-at-risk for hospitalization and mortality due to COVID-19. Thus, efforts should be made to develop and implement preventative programs aimed at minimizing risks among this population.

#### Acknowledgment

The authors have declared that there are no conflicts of interest in relation to the subject of this study. Other financial relations are as follows: Prof. A.D.C. received research grants from Janssen, Novartis, AbbVie, Janssen and Sanofi. Prof. A.D.C. served as a consultant, advisor or speaker to AbbVie, Amgen, Boehringer Ingelheim, Dexcel pharma, Janssen, Kamedis, Lilly, Neopharm, Novartis, Perrigo, Pfizer, Rafa, Samsung Bioepis, Sanofi, Sirbal and Taro. Dr. D.T.B. received an independent research grant from Pfizer in the field of dermatology. All other authors have no other financial relations to declare.

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