Disparities in Intensive Care Unit Admission and Mortality Among Patients With Schizophrenia and COVID-19: A National Cohort Study

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Patients with schizophrenia (SCZ) represent a vulnerable population who have been understudied in COVID-19 research. We aimed to establish whether health outcomes and care differed between patients with SCZ and patients without a diagnosis of severe mental illness. We conducted a population-based cohort study of all patients with identified COVID-19 and respiratory symptoms who were hospitalized in France between February and June 2020. Cases were patients who had a diagnosis of SCZ. Controls were patients who did not have a diagnosis of severe mental illness. The outcomes were in-hospital mortality and intensive care unit (ICU) admission. A total of 50 750 patients were included, of whom 823 were SCZ patients (1.6%). The SCZ patients had an increased in-hospital mortality (25.6% vs 21.7%; adjusted OR 1.30 [95% CI, 1.08–1.56], *P* = .0093) and a decreased ICU admission rate (23.7% vs 28.4%; adjusted OR, 0.75 [95% CI, 0.62–0.91], *P* = .0062) compared with controls. Significant interactions between SCZ and age for mortality and ICU admission were observed (*P* = .0006 and *P* < .0001). SCZ patients between 65 and 80 years had a significantly higher risk of death than controls of the same age (+7.89%). SCZ patients younger than 55 years had more ICU admissions (+13.93%) and SCZ patients between 65 and 80 years and older than 80 years had less ICU admissions than controls of the same age (−15.44% and −5.93%, respectively). Our findings report the existence of disparities in health and health care between SCZ patients and patients without a diagnosis of severe mental illness. These disparities differed according to the age and clinical profile of SCZ patients, suggesting the importance of personalized COVID-19 clinical management and health care strategies before, during, and after hospitalization for reducing health disparities in this vulnerable population.

Introduction

By July 2020, approximately 30 000 French individuals had died from the SARS-CoV-2/coronavirus disease 2019 (COVID-19) infection, placing France in the absolute fifth place in the world behind the United States (130 000), Brazil (60 000), the United Kingdom (43 000), and Italy (34 000). The speed of the pandemic expansion and the risk of saturation of intensive care units (ICUs) led the French government to pronounce confinement for 2 months between mid-March and mid-May 2020. During this period, several regions were particularly affected by saturation of ICUs, such as the Paris Ile-de-France area and the northeast. This saturation may have led some services to "sort" patients, choosing those who were admitted to ICUs while being aware that patients admitted with respiratory failure could not be released from their respirators for several weeks. Learning the lessons of this first wave is crucial in anticipating another potential health crisis.

Schizophrenia (SCZ) patients are a population at particular risk of poor outcomes in COVID-19 infection. A recent Korean study has found SCZ to be associated with an increased risk of severe COVID-19 infection.[1] SCZ individuals have multiple comorbidities that have been identified as risk factors for severe COVID-19[1]: diabetes, hypertension, chronic obstructive respiratory disease, and end-stage renal disease. Previous studies have also shown reduced access to critical care for SCZ patients.[2,3] More information is thus needed to determine whether COVID-19 patients with SCZ have the same

health outcomes and care delivered as patients without a diagnosis of severe mental illness.

We aimed to establish whether health outcomes and care differed between patients with SCZ and patients without a diagnosis of severe mental illness. The primary objective was to compare in-hospital mortality between SCZ patients and patients without a diagnosis of severe mental illness after adjustment for main confounding factors (ie, sociodemographic data, clinical data at baseline, stay data, management data, hospital data, and geographical areas of hospitalization). The secondary objective was to compare ICU admissions between SCZ patients and patients without a diagnosis of severe mental illness.

Methods

Study Design and Data Sources

In this population-based cohort study, we used data from Programme de Médicalisation des Systèmes d'Information (PMSI database), the French national hospital database in which administrative and medical data are systematically collected for acute and psychiatric care. The PMSI database is based on diagnosis-related groups, with all diagnoses coded according to the 10th revision of the International Classification of Diseases (ICD-10) and procedural codes from the Classification Commune des Actes Médicaux (CCAM). In our study, we included all hospitalized patients between February 1, 2020, and June 9, 2020, aged 15 years or older with identified COVID-19 (ICD-10 codes: U07.10 or U07.12 or U07.14) and respiratory symptoms (ICD-10 = U07.10 or U07.11) and a length of hospital stay > 24 h (in order not to take into account pauci- or asymptomatic COVID-19 forms that did not actually require hospitalization) except if the patients died within 24 h. We excluded patients with a severe mental illness diagnosis other than SCZ: bipolar disorder or recurrent major depression (ICD-10 codes = F30* or F31* or F33*).

The PMSI database is used to determine financial resources and is frequently and thoroughly verified by both its producer and the paying party, with possible financial and legal consequences.[4] Data from the PMSI database are anonymized and can be reused for research purposes.[2,5] Due to its suitable accuracy and exhaustive data collection, no patients were lost to follow-up during the study period.

Procedures

We defined 2 populations. Cases were patients who had a diagnosis of SCZ according to specific ICD-10 codes (ie, F20*, F22*, or F25*) in either the acute care or psychiatric PMSI database. Controls were patients who did not have a diagnosis of severe mental illness according to specific ICD-10 codes in the acute care PMSI database and who were not listed in the PMSI psychiatry database.

The primary outcome was in-hospital mortality. The secondary outcome was ICU admission. We gathered patients' sociodemographic data (age classes: <55, 55–65, 65–80, and >80 years; sex; social deprivation: favored/deprived[6]), clinical data at baseline (smoking status: yes/no; overweight and obesity: yes/no; Charlson Comorbidity Index score[7] and main comorbidities: yes/no), stay data (origin of patients: from home or from hospital-institution; length of ICU and hospital stay), management data (Simplified Acute Physiology Score II (SAPS II) for ICU stay; recourse to mechanical ventilation: yes/no; recourse to renal replacement therapy: yes/no), hospital data (hospital category: public, university, or private; number of hospital stays for COVID-19), and geographical areas of hospitalization (4 areas grouped according to pandemic exposure from the highest to the lowest: Ile-de-France, northeast, southeast, and west, data from Sante Publique France: supplementary figure S1).

Statistical Analysis

Continuous variables are expressed as medians and interquartile ranges. Categorical variables are summarized as counts and percentages. No imputation was made for missing data.

The 2 outcomes were assessed with unadjusted (model 1) and multivariable (models 2 and 3) models. Univariable and multivariable generalized linear models with random effects and correlation matrices (to take into account the clustered effect of the hospitals) were used to estimate the association between SCZ and the 2 outcomes.

Model 2 incorporated sociodemographic data (ie, age, sex, social deprivation), clinical data at baseline (ie, smoking status, overweight and obesity, Charlson Comorbidity Index), stay data (ie, origin of the patient), hospital data (ie, hospital category, number of hospital stays for COVID-19), and geographical areas of hospitalization (ie, Ile-de-France, northeast, southeast, and west).

Model 3 incorporated model 2 plus 2 interaction terms, SCZ × age and SCZ × geographical areas of hospitalization, to check whether the association between SCZ and the 2 outcomes was homogenous across ages and geographical areas of hospitalization according to pandemic exposure. The 2 interactions were determined based on a previous work reporting the influence of age and overcrowding on the COVID-19 prognosis.[8] In addition to aggregate analysis, we conducted stratified analyses when an interaction was statistically significant.

A significance threshold of $P < .05$ was used. All analyses were performed in SAS (version 9.4).

Results

Characteristics of the Patients

During the study period, 50 750 patients were included in the analysis (median age, 71 years [interquartile range,

57–83]; 43.2% female), with 823 SCZ patients (1.6%) and 49 927 non-SCZ patients (figure 1, table 1). SCZ patients were more likely to be female (51.2% vs 43.1%, $P = .0005$), to be younger (predominance of age between 65 and 80 years vs >80 years in controls), to be tobacco smokers (10.1% vs 4.2%, $P < .0001$), to be institutionalized (19.1% vs 9.7%, $P < .0001$), to have dementia (25.2% vs 9.6%, $P < .0001$), to be hospitalized in University hospitals (40.8% vs 33.1%, $P < .0001$), and to have a longer length of hospital stay (median [interquartile range], 11 [6–20] vs 9 [5–16], $P < .0001$) than controls. SCZ patients were less likely to have invasive care (ie, invasive mechanical ventilation: 10.7% vs 13.4%, $P = .0443$ and renal replacement therapy: 2.1% vs 3.6%, $P = .0387$) than controls.

In-Hospital Mortality

The overall in-hospital mortality was 21.8%. The univariable analysis is presented in supplementary table S1. SCZ patients had an increased mortality compared to controls (25.6% vs 21.7%; $P = .0188$) (table 1), confirmed by the multivariable analysis (adjusted OR, 1.30 [95% CI, 1.08–1.56]; $P = .0093$) (table 2). There was a significant interaction between SCZ and age ($P = .0006$), with significantly increased mortality only for SCZ patients between 65 and 80 years (adjusted OR, 1.62 [95% CI, 1.27–2.06]; $P = .0002$). The characteristics of SCZ patients and controls according to age classes are presented in table 3. The difference in in-hospital mortality between SCZ and controls varied with age as follows: <55 years:

+3.65%; 55–65 years: +4.64%; 65–80 years: +7.89%; and >80 years: −3.17% (figure 2). There was no heterogeneity in the interaction between SCZ and geographical areas of hospitalization ($P = .0797$).

ICU Admission

A total of 14 351 patients (28.3%) were admitted to the ICU. The univariable analysis is presented in supplementary table S2. SCZ patients were less frequently admitted to the ICU than controls (23.7% vs 28.4%; $P = .0113$) (table 1), confirmed by the multivariable analysis (adjusted OR, 0.75 [95% CI, 0.62–0.91]; $P = .0062$) (table 2). There was a significant interaction between SCZ and age ($P < .0001$), with more ICU admissions for SCZ patients younger than 55 years (adjusted OR, 1.58 [95% CI, 1.09–2.30]; $P = .0177$) and less ICU admissions for SCZ patients between 65 and 80 years (adjusted OR, 0.53 [95% CI, 0.41–0.70]; $P < .001$) and older than 80 years (adjusted OR, 0.51 [95% CI, 0.29–0.88]; $P = .0168$). The difference in ICU admission between SCZ patients and controls varied with age as follows: <55 years: +13.93%; 55–65 years: −2.84%; 65–80 years: −15.44%; and >80 years: −5.93% (figure 3). There was no heterogeneity in the interaction between SCZ and geographical areas of hospitalization ($P = .0591$).

Discussion

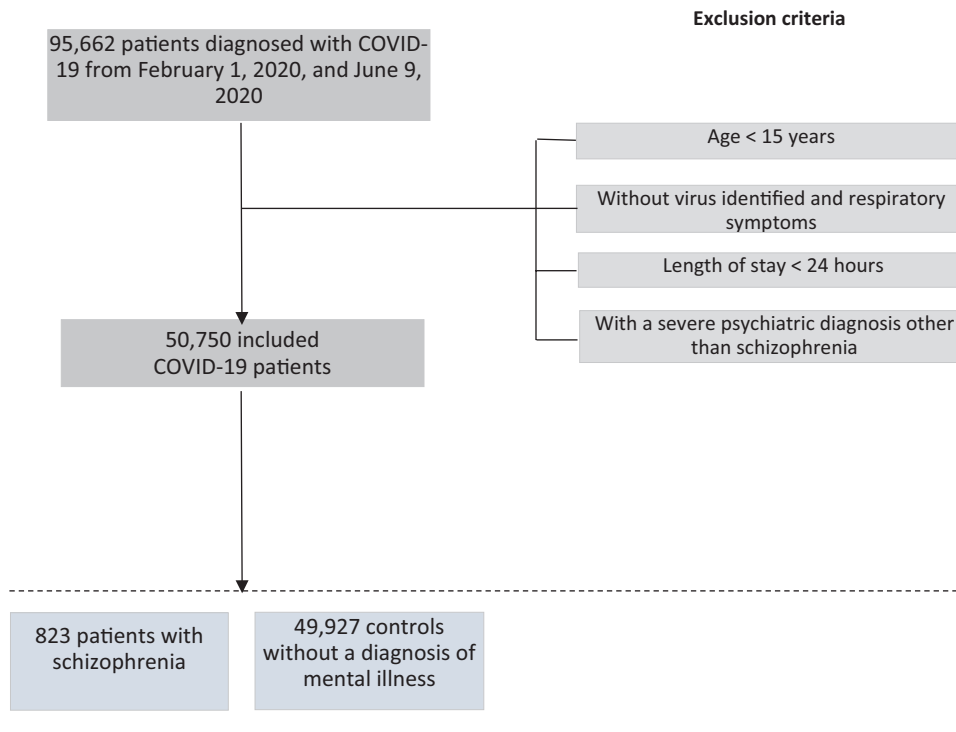To our knowledge, we report the largest series of SCZ patients with COVID-19 to date, including 823 SCZ patients

Fig. 1. Flow chart.

Table 1. Baseline Characteristics and Health Outcomes of Hospitalized COVID-19 Patients With Schizophrenia and Without a Diagnosis of Severe Mental Illness (*n* = 50 750)

Characteristics	Total *n* = 50 750 *n* (%)	SCZ Patients *n* = 823 *n* (%)	Controls *n* = 49 927 *n* (%)	*P* value
Sociodemographic data				
Age				**<.0001**
<55 years	10 538 (20.8)	130 (15.8)	10 408 (20.9)	
55–65 years	8582 (16.9)	134 (16.3)	8448 (16.9)	
65–80 years	15 517 (30.6)	340 (41.3)	15 177 (30.4)	
≥80 years	16 113 (31.7)	219 (26.6)	15 894 (31.8)	
Sex				**.0005**
Male	28 818 (56.8)	402 (48.8)	28 416 (56.9)	
Female	21 932 (43.2)	421 (51.2)	21 511 (43.1)	
Social deprivation index				.1340
More favored	24 681 (48.6)	442 (53.7)	24 239 (48.6)	
More deprived	24 126 (47.6)	351 (42.7)	23 775 (47.6)	
Missing	1943 (3.8)	30 (3.6)	1913 (3.8)	
Clinical data at baseline				
Smoker	2175 (4.3)	83 (10.1)	2092 (4.2)	**<.0001**
Weight[a]				
Overweight and obesity	7201 (14.2)	138 (16.8)	7063 (14.2)	.0576
Comorbidities				
Charlson Comorbidity Index score				.0006
0	20 865 (41.1)	287 (34.9)	20 578 (41.2)	
1–2	17 520 (34.5)	343 (41.7)	17 177 (34.4)	
≥3	12 365 (24.4)	193 (23.4)	12 172 (24.3)	
Renal disease	6125 (12.1)	102 (12.4)	6023 (14.1)	.7687
Peripheral vascular disease	2879 (5.7)	41 (5.0)	2838 (5.7)	.4534
Hemiplegia or paraplegia	2111 (4.2)	40 (4.9)	2151 (4.2)	.3558
Cancer	4482 (8.8)	51 (6.2)	4431 (8.9)	**.0189**
HIV or AIDS	304 (0.6)	5 (0.6)	299 (0.6)	.8935
Diabetes with complications	3112 (6.1)	54 (6.6)	3058 (6.1)	.6975
Diabetes without complications	10 999 (21.7)	154 (18.7)	10 845 (21.7)	.0584
Dementia	4983 (9.8)	207 (25.2)	4776 (9.6)	**<.0001**
Cerebrovascular disease	3191 (6.3)	63 (7.7)	3128 (6.3)	.1324
Chronic obstructive pulmonary disease	6425 (12.7)	122 (14.8)	6303 (12.6)	.0729
Congestive heart failure	8178 (16.1)	110 (13.4)	8068 (16.2)	.0646
Myocardial infarct	3740 (7.4)	38 (4.6)	3702 (7.4)	**.0129**
Stay data				
Origin of the patient				**<.0001**
From home	45 769 (90.2)	666 (80.9)	45 103 (90.3)	
Other (hospital–institution)	4981 (9.8)	157 (19.1)	4824 (9.7)	
Length of hospital stay, median (IQR)—number of days	9 (5–16)	11 (6–20)	9 (5–16)	**<.0001**
Length of ICU stay, median (IQR)—number of days	9 (4–18)	10 (4–18)	9 (4–18)	.6695
Management data				
SAPS II score at ICU admission, median (IQR)	32.0 (22.0–45.0)	31.0 (21.0–46.0)	32.0 (22.0–45.0)	.3799
Recourse to invasive mechanical ventilation	6791 (13.4)	88 (10.7)	6703 (13.4)	**.0443**
Recourse to continuous renal-replacement therapy	1787 (3.5)	17 (2.1)	1770 (3.6)	**.0387**
Hospital data				
Hospital category				.0001
Public	29 837 (58.8)	448 (54.4)	29 389 (58.9)	
University	16 860 (33.2)	336 (40.8)	16 524 (33.1)	
Private	4053 (8.0)	39 (4.8)	4014 (8.0)	
Geographical exposure[b]				.0251
Ile-de-France	18 770 (37.0)	355 (43.1)	18 415 (36.9)	
Northeast	16 314 (32.2)	225 (27.3)	16 089 (32.2)	
Southeast	8381 (16.5)	134 (16.3)	8247 (16.5)	
West	7285 (14.4)	109 (13.2)	7176 (14.4)	
Outcomes				
In-hospital mortality	11 065 (21.8)	211 (25.6)	10 854 (21.7)	**.0188**
ICU admission	14 351 (28.2)	195 (23.7)	14 156 (28.4)	**.0113**

Note: Comorbidities were based on the 10th revision of the International Statistical Classification of Diseases from the Programme de Medicalisation des Systèmes d'Information (PMSI)—French medico-administrative database based on diagnosis-related groups. P value in bold denotes statistical significance. N, effective; ICU, intensive care unit; IQR, interquartile range; SAPS II score, Simplified Acute Physiology Score II; SCZ, schizophrenia.
[a]If the body mass index (BMI) is 18.5 to <25: normal weight; if the BMI is 25.0 to <30: overweight; and if the BMI is 30.0 or higher: obesity.
[b]Geographical exposure: 4 areas were identified with different pandemic exposure from the lowest to the highest: west, southeast, northeast, and Ile-de-France.

Table 2. Associations Between Schizophrenia, In-Hospital Mortality, and ICU Admission (*n* = 50 750)

	In-Hospital Mortality		ICU Admission	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Model 1	1.246 (1.045–1.485)	**.0186**	0.782 (0.653–0.937)	**.0118**
Model 2	1.298 (1.080–1.561)	**.0093**	0.749 (0.619–0.906)	**.0062**
Model 3				
Interaction term, age × SCZ		**.0006***		**<.0001***
<55 years	1.761 (0.912–3.401)	.0905	1.582 (1.087–2.299)	**.0177**
55–65 years	1.577 (0.969–2.571)	.0661	0.919 (0.630–1.340)	.6561
65–80 years	1.621 (1.276–2.062)	**.0002**	0.533 (0.405–0.702)	**<.001**
≥80 years	0.873 (0.657–1.161)	.3429	0.509 (0.294–0.880)	**.0168**
Interaction term, geographical areas of hospitalization × SCZ		.0797*		.0591*

Note: Model 1: unadjusted model. Model 2: adjustment for sociodemographic data (age, sex, social deprivation), clinical data at baseline (smoking status, overweight and obesity, Charlson Comorbidity Index), stay data (origin of the patient), hospital data (hospital category, number of hospital stays for COVID-19), and geographical areas of hospitalization. Model 3: model 2 plus the interaction term age × SCZ. There was no heterogeneity in the interaction between SCZ and geographical areas of hospitalization. *P* value in bold denotes statistical significance. Reference: controls. ICU, intensive care unit; SCZ, schizophrenia.
*P value for interaction.

hospitalized for COVID-19 infection with a nationwide geographical distribution. In this large population-based cohort study, we reported the existence of disparities in health and health care between hospitalized COVID-19 SCZ patients and patients without a diagnosis of severe mental illness. These disparities differed according to the age and clinical profile of SCZ patients.

SCZ patients under 55 years of age had 14% more ICU admissions than patients without a diagnosis of severe mental illness, suggesting more severe COVID-19 infection in SCZ patients.

SCZ patients under 55 years were mostly male, were more frequently smokers, were more overweight and obese, and had more multiple somatic comorbidities, including chronic obstructive pulmonary disease, than patients without a diagnosis of severe mental illness. Although the results are contradictory, smoking seems more likely to be associated with the negative progression and adverse outcomes of COVID-19.[9] Obesity in patients younger than 60 years has been reported as a risk factor for COVID-19 hospital admission and worse outcomes.[10] Chronic obstructive pulmonary disease has been also reported to worsen the progression and prognosis of COVID-19.[11] A delay in access to hospital care may be evoked to explain the severity of SCZ patients although we do not have any prehospital data. The existence of barriers in access to somatic care for SCZ patients has been described in previous studies.[2,10,12,13] Altogether, these findings suggest that young SCZ patients with the risk factors listed above should be targeted as a high-risk population for early intervention.[14,15]

These discrepancies in severity are apparently compensated by the important increase in ICU admissions that prevented increased mortality in SCZ patients. However, depression, anxiety, post-traumatic stress disorder, and cognitive dysfunction are increasingly recognized among patients who survive an ICU admission and these consequences have a significant impact on the patient's long-term quality of life.[16] Rehabilitation following critical illness has shown its efficacy to improve both physical and nonphysical recovery,[17] and SCZ patients should benefit from these programs.

SCZ patients between 65 and 80 years had a higher risk of death (+7.89%), and SCZ patients between 65 and 80 years and over 80 years old had less ICU admissions than patients without a diagnosis of severe mental illness (−15.44% and −5.93%, respectively).

SCZ patients between 65 and 80 years were mostly female, had more dementia, and had more cerebrovascular disease than patients without a diagnosis of severe mental illness. Previous studies have confirmed the relationship between SCZ and dementia risk, especially in women.[18,19] The diagnosis of dementia has been reported as an important risk factor for mortality in COVID-19 patients.[20,21] Dementia has also been associated with increased aggressive behavior in institutionalized patients who may affect the care of these patients at the hospital.[22] In addition, a new environment can lead to increased stress and behavioral problems.[23] Delirium caused by hypoxia could complicate the presentation of dementia.[24] Dementia as a preexisting condition may in part explain the lower ICU admissions in SCZ patients. All these elements demonstrate the importance of reinforcement of inpatient support for SCZ patients with dementia. To date, psychogeriatric teams remain insufficiently developed while demand in the aging population is growing.

SCZ patients between 65 and 80 years were more frequently referred from hospitals or institutions than patients without a diagnosis of severe mental illness, which can explain the poor health outcomes in SCZ patients. A French study reported that most psychiatric inpatients with a COVID-19 diagnosis were kept in dedicated

Table 3. Baseline Characteristics of Hospitalized COVID-19 Patients With Schizophrenia and Without a Diagnosis of Severe Mental Illness by Age Classes (n = 50 750)

Age Classes	<55 years			55–65 years			65–80 years			≥80 years		
	SCZ	Controls		SCZ	Controls		SCZ	Controls		SCZ	Controls	
	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)		n (%)	n (%)	
Characteristics	n = 130	n = 10 408	P value	n = 134	n = 8448	P value	n = 340	n = 15 177	P value	n = 219	n = 15 894	P value
Sociodemographic data												
Sex			.1766			**.0327**			**.0002**			**.0041**
Male	82 (63.1)	5910 (56.8)		73 (54.5)	5458 (64.6)		168 (49.4)	9701 (63.9)		75 (34.3)	7347 (46.2)	
Female	48 (36.9)	4498 (43.2)		61 (45.5)	2990 (35.4)		172 (50.6)	5476 (36.1)		144 (65.7)	8547 (53.8)	
Social deprivation index			.8309			.2608			.2553			.3974
More favored	66 (50.8)	5222 (50.2)		74 (55.2)	4123 (48.8)		177 (52.0)	7047 (46.4)		125 (57.1)	7847 (49.4)	
More deprived	60 (46.2)	4754 (45.7)		61 (45.6)	3968 (47.0)		146 (43.0)	7550 (50.0)		88 (40.2)	7503 (47.2)	
Missing	4 (3.0)	432 (4.1)		3 (2.2)	357 (4.2)		17 (5.0)	580 (3.6)		6 (2.7)	544 (3.4)	
Clinical data at baseline												
Smoker	27 (20.8)	376 (3.6)	**<.0001**	20 (14.9)	496 (5.9)	**.0013**	6 (1.8)	640 (4.2)	**.0231**	5 (2.3)	325 (2.0)	.7926
Weight[a]			**.0018**			.7467			.6550			.0896
Overweight and obesity	47 (36.2)	2228 (21.4)		25 (18.7)	1673 (19.8)		48 (14.1)	2290 (15.1)		18 (8.2)	872 (5.5)	
Comorbidities												
Charlson Comorbidity Index score			**.0043**			.0849			**.0465**			.2040
0	69 (53.1)	7071 (67.9)		56 (41.8)	4269 (50.5)		119 (35.0)	5265 (34.7)		43 (19.6)	3973 (25.0)	
1–2	49 (37.7)	2507 (24.1)		55 (41.0)	2686 (31.8)		142 (41.8)	5512 (36.3)		97 (44.3)	6472 (40.7)	
≥3	12 (9.2)	830 (8.0)		23 (17.2)	1493 (17.7)		79 (23.2)	4400 (29.0)		79 (36.1)	5449 (34.3)	
Renal disease	4 (3.1)	374 (3.6)	.7586	11 (8.2)	553 (6.6)	.4569	33 (9.7)	1897 (12.5)	.1265	54 (24.7)	3199 (20.1)	.1202
Peripheral vascular disease	1 (0.8)	100 (1.0)	.8285	3 (2.2)	299 (3.5)	.4389	22 (6.5)	1139 (7.5)	.5214	15 (6.9)	1300 (8.2)	.5201
Hemiplegia or paraplegia	5 (3.9)	262 (2.5)	.3623	10 (7.5)	352 (4.2)	.0907	16 (4.7)	811 (5.3)	.6597	9 (4.1)	686 (4.3)	.8862
Cancer	5 (3.9)	305 (2.9)	.5542	8 (6.0)	658 (7.8)	.4516	23 (6.8)	681 (4.5)	**.0098**	15 (6.9)	1623 (10.2)	.1110
HIV or AIDS	1 (0.8)	126 (1.2)	.6617	2 (1.5)	111 (1.3)	.8606	2 (0.6)	58 (0.4)	.6986	0 (0.0)	4 (0.0)	
Diabetes with complications	4 (3.1)	201 (1.9)	.3680	10 (7.5)	449 (5.3)	.2970	27 (7.9)	1338 (8.8)	.4361	13 (5.9)	1070 (6.7)	.6127
Diabetes without complications	19 (14.6)	1267 (12.2)	.4156	20 (14.9)	1898 (22.5)	.0620	78 (22.9)	4285 (28.2)	**.0476**	37 (16.9)	3395 (21.4)	.1530
Dementia	3 (2.3)	16 (0.2)	**.0051**	7 (5.2)	77 (0.9)	**.0017**	78 (22.9)	829 (5.5)	**<.0001**	119 (54.3)	3854 (24.3)	**<.0001**
Cerebrovascular disease	2 (1.5)	150 (1.4)	.9283	5 (3.7)	343 (4.1)	.8514	34 (10.0)	1024 (6.8)	**.0403**	22 (10.1)	1611 (10.1)	.9169
Chronic obstructive pulmonary disease	27 (20.8)	933 (9.0)	**.0008**	24 (17.9)	931 (11.0)	**.0288**	53 (15.6)	2382 (15.7)	.9839	18 (8.2)	2057 (12.9)	.0628
Congestive heart failure	8 (6.2)	281 (2.7)	**.0400**	11 (8.2)	636 (7.5)	.7724	43 (12.7)	2462 (16.22)	.1155	48 (21.9)	4689 (29.50)	**.0350**
Myocardial infarct	5 (3.9)	130 (1.3)	**.0304**	4 (3.0)	425 (5.0)	.3079	11 (3.2)	1410 (9.3)	**.0036**	18 (8.2)	1737 (10.9)	.2605
Stay data												
Origin of the patient			**.0260**			**.0062**			**.0002**			**.0002**
From home	117 (90.0)	9894 (95.1)		115 (85.8)	7890 (93.4)		277 (81.5)	13 746 (90.6)		157 (71.7)	13 573 (85.4)	
Other (hospital-institution)	13 (10.0)	514 (4.9)		19 (14.2)	558 (6.6)		63 (18.5)	1431 (9.4)		62 (28.3)	2321 (14.6)	

Table 3. Continued

Age Classes	<55 years			55–65 years			65–80 years			≥80 years		
	SCZ	Controls		SCZ	Controls		SCZ	Controls		SCZ	Controls	
Characteristics	n (%)	n (%)	P value	n (%)	n (%)	P value	n (%)	n (%)	P value	n (%)	n (%)	P value
	n = 130	n = 10 408		n = 134	n = 8448		n = 340	n = 15 177		n = 219	n = 15 894	
Length of hospital stay, median (IQR)—number of days	10.0 (5.0–16.0)	6.0 (3.0–11.0)	**.0006**	12.0 (7.0–15.0)	9.0 (5.0–16.0)	**<.0001**	10.5 (6.0–19.0)	11.0 (6.0–18.0)	.0611	11.0 (5.0–20.0)	10.0 (5.0–17.0)	**.0021**
Length of ICU stay, median (IQR)—number of days	7.0 (4.0–17.0)	7.0 (3.0–16.0)	.7034	14.0 (9.0–20.0)	9.0 (4.0–19.0)	.1016	8.0 (3.0–15.0)	10.0 (5.0–20.0)	0.1302	12.0 (9.0–17.0)	6.0 (2.0–11.0)	**.0004**
Management data												
SAPS II score at ICU admission, median (IQR)	27.5 (19.0–40.5)	24.0 (15.0–36.0)	.3940	34.5 (23.0–44.5)	31.0 (22.0–43.0)	.9193	32.0 (22.0–50.0)	37.0 (27.0–50.0)	.0590	28.0 (0.0–51.0)	32.0 (0.0–42.0)	.8248
Recourse to invasive mechanical ventilation	27 (20.8)	1416 (13.6)	**.0376**	28 (20.9)	1801 (21.3)	.9075	30 (8.8)	3122 (20.6)	**.0003**	3 (1.4)	364 (2.3)	.4023
Recourse to continuous renal-replacement therapy	4 (3.1)	301 (2.9)	.9024	5 (3.7)	400 (4.7)	.5977	5 (1.5)	836 (5.5)	**.0112**	3 (1.4)	233 (1.5)	.8879
Hospital data												
Hospital category			.2472			.8862			**.0075**			**<.0001**
Public	72 (55.3)	5742 (55.2)		74 (55.2)	4773 (56.5)		199 (**58.5**)	8912 (58.7)		103 (47.0)	9962 (62.7)	
University	53 (40.8)	3850 (37.0)		50 (37.3)	2990 (35.4)		128 (37.7)	4957 (32.7)		105 (48.0)	4727 (29.7)	
Private	5 (3.9)	816 (7.8)		10 (7.5)	685 (8.1)		13 (3.8)	1308 (8.6)		11 (5.0)	1205 (7.6)	
Geographical exposure[b]			.1433			.9355			.1529			**.0320**
Ile-de-France	57 (43.9)	4635 (44.5)		52 (38.8)	3501 (41.4)		152 (44.7)	5119 (33.7)		94 (42.9)	5160 (32.5)	
Northeast	46 (35.4)	2763 (26.6)		41 (30.6)	2501 (29.6)		84 (24.7)	5276 (34.8)		54 (24.7)	5549 (34.9)	
Southeast	16 (12.3)	1562 (15.0)		22 (16.4)	1284 (15.2)		59 (17.4)	2497 (16.5)		37 (16.9)	2904 (18.3)	
West	11 (8.4)	1448 (13.9)		19 (14.2)	1162 (13.8)		45 (13.2)	2285 (15.0)		34 (15.5)	2281 (14.3)	

Note: Comorbidities were based on the 10th revision of the International Statistical Classification of Diseases from the Programme de Medicalisation des Systèmes d'Information (PMSI)–French medico-administrative database based on diagnosis-related groups. *N*, effective; ICU, intensive care unit; IQR, interquartile range; SAPS II score, Simplified Acute Physiology Score II; SCZ, schizophrenia. *P* value in bold denotes statistical significance.

[a]If the body mass index is 18.5 to <25: normal weight; if the BMI is 25.0 to <30: overweight; and if the BMI is 30.0 or higher: obesity.

[b]Geographical exposure: 4 areas were identified with different pandemic exposure from the lowest to the highest: west, southeast, northeast, and Ile-de-France.
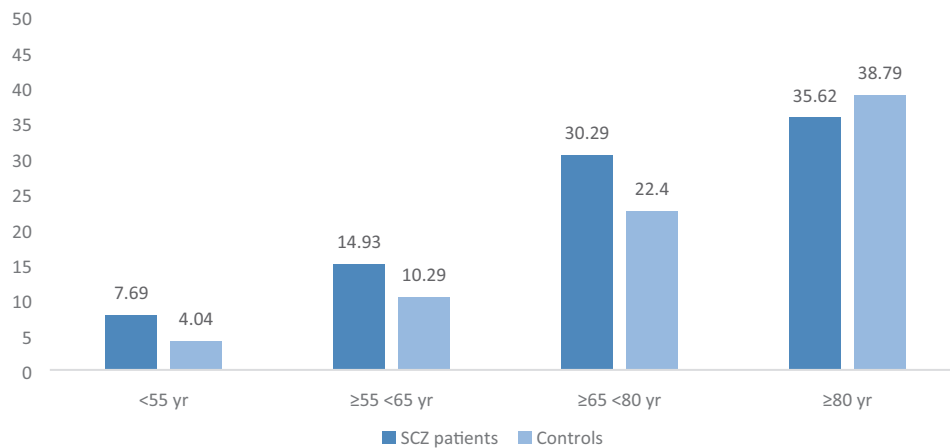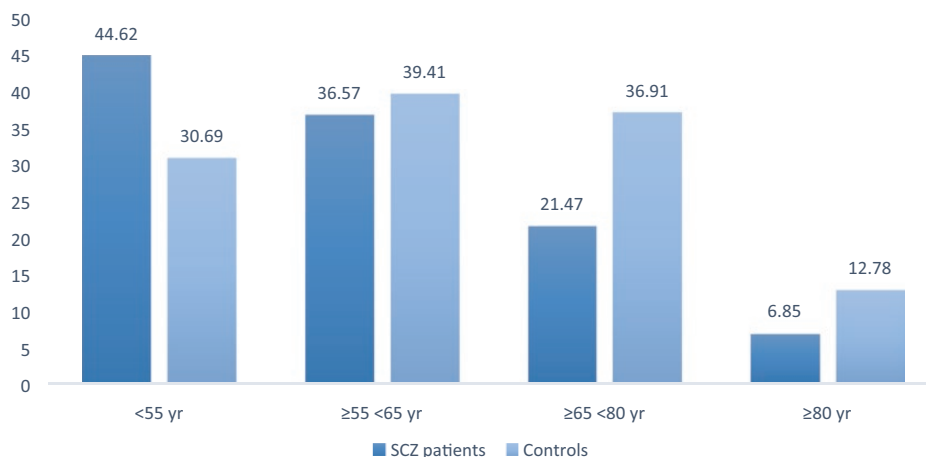
<55 year: p=0.0643

≥55 and <65 year: p=0.1083

≥65 and <80 year: p=0.0063

>80 year: p=0.3762

Fig. 2. In-hospital mortality by age classes. <55 years: P = .0643; ≥55 and <65 years: P = .1083; ≥65 and <80 years: P = .0063; >80 years: P = .3762.

<55 year: p=0.0055

≥55 and <65 year: p=0.5175

≥65 and <80 year: p<0.0001

>80 year: p=0.0246

Fig. 3. ICU admission by age classes. <55 years: P = .0055; ≥55 and <65 years: P = .5175; ≥65 and <80 years: P < .0001; >80 years: P = .0246.

psychiatric departments and not in general hospitals.[25] The division between physical and psychiatric medicine results in confusion about which sector of the health service (ie, primary, mental health, or acute care levels) should take responsibility for the management of patients with complex health needs.[10] We lack national data on the rate of elderly SCZ patients who are institutionalized, yet we can reasonably hypothesize that institutionalization

is a risk factor for COVID-19 severe infection in elderly patients with SCZ. Our results support a strategy of systematic detection in institutionalized SCZ patients and early intervention in this population. This has already been done in a homeless shelter in Boston where 36% of the residents tested positive.[26]

The lower ICU admission rate in SCZ patients than in patients without a diagnosis of severe mental illness is a perfect illustration of the debate between utility- and equity-based arguments.[27] SCZ patients had one of the poorest prognosis indicators justifying ICU triage. However, this triage based solely on prognosis exacerbates existing health inequities, leaving disadvantaged patients worse off. Factors consistently found in the literature to be associated with a decision to admit or refuse a patient to the ICU are age, severity of illness and functional status at baseline, initial ward or team the patient was referred from, bed availability, and do-not-resuscitate order status/patient preference.[28] Although some factors are not modifiable (eg, age, functional status), others can be improved so as not to penalize SCZ patient ICU admission. The first one is to guarantee respect for the SCZ patient's wishes and values expressed directly by the patient via advance directives or reported by relatives. However, the overrepresentation of institutionalized SCZ patients and dementia patients suggests an autonomy loss and probably increased social isolation of these patients. The absence of relatives may have impacted medical decisions of do-not-resuscitate orders, and a previous study has suggested that patients with severe mental illness may be more prone to ask for do-not-resuscitate orders than those without psychiatric disorders.[29] Previous works have reported that implementation of advance directives is difficult in patients with psychiatric disorders.[30] Efforts should be undertaken to embed the use of advance directives in routine mental health care.[31] Second, the link between the hospital and/or the ICU team and the initial ward or team the patient was referred from needs to be strengthened. A psychiatrist on call must be reachable 24/7 to participate, if necessary, in a collegial decision to not admit the patient to the ICU. Third, as previously noted, the time of access to the hospital is a major issue and must be kept to a minimum as a condition to prevent patients from being admitted with very serious conditions. Finally, mental illness stigma may also play a specific role in the lower ICU admission rate of SCZ patients from nursing homes and psychiatric departments.[32] ICUs may be less prone to admit a patient referred by a psychiatric department due to potential behavioral/aggressive disturbances of SCZ patients and the inability to monitor them properly. Some ICU staff report being unprepared to care for patients with severe mental illness.[33] ICU staff should be specifically trained for the care of patients with severe mental illness.

Geographical areas of hospitalization did not influence the relationship between SCZ and mortality or ICU admission. We could have expected that access to care and health outcomes would be influenced in SCZ patients according to hospital overcrowding. However, our data may have been insufficiently accurate, and further studies will need to work with more accurate indicators such as bed occupancy rates at the hospital or ICU level.

Limits and Perspectives

The worldwide absolute mortality data suggest that COVID-19 infection may have different impacts across countries due to multiple factors (climate, facility organization, COVID-19 public management strategies). Thus, our results may not be extrapolated to other countries and should be replicated. Some data are known to be insufficiently coded in the medicoadministrative databases (eg, smoking, overweight, and obesity). We have no information on the contamination rate of SCZ patients[34] and the delay between the onset of infection and hospitalization. Treatment variables including psychotropics and repurposed or experimental anti-COVID-19 treatments were not available in the PMSI database. Some experimental anti-COVID-19 treatments may have been contraindicated in SCZ patients because of potential interactions with psychotropics.[35–38] No biological data are available in the PMSI database and SCZ has been shown to have different immune-inflammatory profiles[39] that may also partly explain the observed differences. Further studies should be carried out to explore the influence of these data on the prognosis of COVID-19 in SCZ patients. Finally, we do not know if our results are specific to COVID-19 or if they would be similar in other urgent pathologies. Future studies should explore this issue.

Conclusion

This study reports the existence of disparities in health and health care between hospitalized COVID-19 SCZ patients and patients without a diagnosis of severe mental illness. These disparities differed according to the age and clinical profile of SCZ patients, suggesting the importance of personalized COVID-19 clinical management and health care strategies before, during, and after hospitalization for reducing health disparities in this vulnerable population.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin*.

Figure S1. Geographical areas of hospitalization grouped according to pandemic exposure from the highest to the lowest: Ile-de-France, northeast, southeast and west; data from Sante Publique France. Peak of the epidemic in France: 04/04/2020. https://www.gouvernement.fr/info-coronavirus/carte-et-donnees.

Table S1. Factors associated with in-hospital mortality: Univariate analysis (n = 50 750). *If the body mass index (BMI) is 18.5 to <25: normal weight; if the BMI is 25.0 to <30: overweight; and if the BMI is 30.0 or higher: obesity. **Geographical exposure: 4 areas were identified with different pandemic exposure from the lowest to the highest: west, southeast, northeast and Ile-de-France. N: effective; %: percentage; ICU: intensive care unit; IQR: interquartile range; SAPS II score: Simplified Acute Physiology Score II; SCZ: schizophrenia. Comorbidities were based on the 10th revision of the International Statistical Classification of Diseases from the Programme de Medicalisation des Systèmes d'Information (PMSI)—French medico-administrative database based on diagnosis related-groups (DRG). P-value in bold: statistical significance.

Table S2. Factors associated with ICU admission: Univariate analysis (n = 50 750). *If the body mass index (BMI) is 18.5 to <25: normal weight; if the BMI is 25.0 to <30: overweight; and if the BMI is 30.0 or higher: obesity. **Geographical exposure: 4 areas were identified with different pandemic exposure from the lowest to the highest: west, southeast, northeast and Ile-de-France. N: effective; %: percentage; ICU: intensive care unit; IQR: interquartile range; SAPS II score: Simplified Acute Physiology Score II; SCZ: schizophrenia. Comorbidities were based on the 10th revision of the International Statistical Classification of Diseases from the Programme de Medicalisation des Systèmes d'Information (PMSI) – French medico-administrative database based on diagnosis related-groups (DRG). P-value in bold: statistical significance.

Author Contributions

V.O. and V.P. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: L.B., G.F. Acquisition, analysis, or interpretation of data: P.A., K.B., L.B., C.L., P.-M.L., A.L., G.F., M.L., V.P., V.O. Drafting of the manuscript: L.B., G.F. Critical revision of the manuscript for important intellectual content: all the authors. Statistical analysis: V.P. Administrative, technical, or material support: V.O. Supervision: L.B.

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