Research paper

Psychiatric disorders among hospitalized patients deceased with COVID-19 in Italy

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A R T I C L E   I N F O

A B S T R A C T

Background: there is concern about the increased risk for SARS-CoV-2 infection, COVID-19 severe outcomes and disparity of care among patients with a psychiatric disorder (PD). Based on the Italian COVID-19 death surveillance, which collects data from all the hospitals throughout the country, we aimed to describe clinical features and care pathway of patients dying with COVID-19 and a preceding diagnosis of a PD.

Methods: in this cross-sectional study, the characteristics of a representative sample of patients, who have died with COVID-19 in Italian hospitals between February 21st and August 3rd 2020, were drawn from medical charts, described and analysed by multinomial logistic regression according to the recorded psychiatric diagnosis: no PD, severe PD (SPD) (i.e. schizophrenia and other psychotic disorders, bipolar and related disorders), common mental disorder (CMD) (i.e. depression without psychotic features, anxiety disorders).

Findings: the 4020 COVID-19 deaths included in the study took place in 365 hospitals across Italy. Out of the 4020 deceased patients, 84 (2•1%) had a previous SPD, 177 (4.4%) a CMD. The mean age at death was 78.0 (95%CI 77.6−78.3) years among patients without a PD, 71.8 (95%CI 69.3−72.0) among those with an SPD, 79.5 (95%CI 78.0−81.1) in individuals with a CMD. 2253 (61.2%) patients without a PD, 62 (73.8%) with an SPD, and 136 (78.2%) with a CMD were diagnosed with three or more non-psychiatric comorbidities.

When we adjusted for clinically relevant variables, including hospital of death, we found that SPD patients died at a younger age than those without a PD (adjusted OR per 1 year increment 0.96; 95% CI 0.94−0.98). Women were significantly more represented among CMD patients compared to patients without previous psychiatric history (aOR 1.56; 95% CI 1.05−2.32). Hospital admission from long-term care facilities (LTCFs) was strongly associated with having an SPD (aOR 9.02; 95% CI 4.99−16.3) or a CMD (aOR 2.09; 95% CI 1.19−3.66). Comorbidity burden, fever, admission to intensive care and time from symptoms' onset to nasopharyngeal swab did not result significantly associated with an SPD or with a CMD in comparison to those without any PD.

Interpretation: even where equal treatment is in place, the vulnerability of patients with a PD may reduce their chance of recovering from COVID-19. The promotion of personalised therapeutic projects aimed at including people with PD in the community rather than in non-psychiatric LTCFs should be prioritised.

1. Introduction

As of 16th February 2021, 109,190,723 COVID-19 cases and 2,409,381 COVID-19 related deaths have been registered worldwide [1]. The awareness of the epidemic's differential impact has

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Research in context

Evidence before this study

The inclusion/exclusion criteria for the online literature search included primary research about people with a previous diagnosis of a psychiatric disorder dying with COVID-19 published from Jan 1 to Dec 14, 2020. The search covered PubMed and ProQuest databases. The core search strategy included both key- and text-words to find all possible relevant articles (*mental disorders, mental*, psychiatr*, diagnosis, "pre-existing", previous, antecedent, preced*, earlier, anterior, mortality, dead, death, deaths, die, dying, SARS-CoV-2, COVID*, "new coronavirus")*.

A case-control and two cohort electronic health record studies found a higher risk for COVID-19 diagnosis, and two of them for COVID-19 related mortality among patients with a psychiatric disorder compared to individuals without a psychiatric history. We retrieved a single retrospective observational study giving details of older inpatients in psychiatric wards during the peak of the COVID-19 London pandemic. The study found a higher risk of SARS-CoV-2 infection and a higher proportion of COVID-19 related deaths among psychiatric inpatients than in the community, registering an alarming delay in making testing and personal protective equipment available among patients in psychiatric hospitals, compared to patients admitted to other settings.

Added value of this study

To our best knowledge, this is the first national study providing detailed clinical characteristics and care pathways of patients with a psychiatric diagnosis who have died in hospital with COVID-19. In Italy, patients with a severe psychiatric disorder were found to die at a younger age compared to other inpatients. Women were more represented among dead patients with a common mental disorder compared to dead patients with no psychiatric disorders. Patients with a psychiatric diagnosis were more often admitted to hospital from long-term care facilities (LTCFs) compared to patients without a psychiatric history.

SARS-CoV-2 testing and access to intensive care of critically ill COVID-19 patients were assured to patients with and without a psychiatric diagnosis without disparity.

Implications of all the available evidence

Existing evidence shows that a psychiatric history might be an independent risk factor for SARS-CoV-2 infection and COVID-19 mortality. Consistently, some countries have included patients with severe mental illness in the priority COVID-19 vaccination group.

Among the characteristics of patients deceased with COVID-19 and a psychiatric diagnosis described by our study, living in non-psychiatric LTCFs is the one on which we can act promptly. It is urgent to reconsider mental health care pathways in the pandemic scenario. Home− and community-based personalised therapeutic rehabilitation care for people with mental health needs and general condition of fragility should be promoted to the greatest possible extent.

and suicidal ideation as compared to healthy controls during the peak of the COVID-19 epidemic in China [3]. Among patients with a psychiatric disorder (PD), reduced awareness of risk and poor adherence to personal protection measures, medical comorbidities, delay in receiving treatment because of difficulty in recognizing or reporting physical symptoms due to cognitive or motivational impairments, socioeconomic disadvantages, and care barriers are possible factors leading to an increased risk of SARS-CoV-2 infection and severe COVID-19 [4,5]. Clusters of COVID-19 cases and deaths were described in large psychiatric hospitals [6]. Indeed, long-term care facilities (LTCFs), where the prevalence of PDs among resident is relatively high [7], registered a high COVID-19 morbidity and mortality [8]. Despite a broad consensus on these issues, only a few studies focused on patients with PDs and confirmed COVID-19.

A medical record review described a higher mortality rate among patients with a prior psychiatric diagnosis hospitalised for COVID-19 compared to those without a psychiatric condition in the Northeast of the United States [9]. A larger electronic health records case-control study found that the odds of being diagnosed with COVID-19 were 7 to 10 times higher for patients with a diagnosis of depression, schizophrenia and bipolar disorder in the previous year [10]. Moreover, the death rate was higher in COVID-19 patients with a mental disorder compared to COVID-19 patients with no mental disorder [10]. Another study analysing data from 69 million individuals in the USA, found that having a recorded diagnosis of PD was associated with a 65% increased risk of COVID-19 diagnosis, compared to a matched cohort without a psychiatric diagnosis [11]. Finally, a retrospective observational study was performed among older inpatients psychiatric population and patients with young-onset dementia in psychiatric wards during the peak of the London COVID-19 pandemic [12]. The alarming delay in providing testing and personal protective equipment to patients in psychiatric hospitals, where 82% of the patients with COVID-19 were compulsory detained, compared to patients admitted locally with physical illnesses, calls for urgent actions to overcome this disparity [12].

The Italian mental health service celebrated 40 years without mental hospitals in 2018 [13]. In fact, the Italian psychiatric reform (1978) established that patients with mental disorders have the right to be treated as the patients with non-psychiatric disorders/diseases. Acute mental health conditions are managed in psychiatric wards not exceeding 15 beds located in general hospitals, while community residential facilities host patients requiring long-term care [13]. Compulsory admissions accounted for less than 5% of the national psychiatric admissions in 2015 [13].

Italy had the second largest number of COVID-19 cases after China and a very high case-fatality rate in March 2020 [14]. The challenge to the National Health Service has been immense [15]. For instance, 67% of the 720 intensive care beds were required to treat patients with COVID-19 in the first 18 days of the epidemic in Lombardy, the Region most severely hit by the SARS-CoV-2 outbreak [15].

So far, limited data are available on characteristics of patients with PDs who died with COVID-19. The present study aimed at describing, in patients who died with COVID-19 in Italian hospitals, the clinical presentation, course, management and care pathway of patients with a prior psychiatric diagnosis compared to those with no previous psychiatric history.

2. Methods

2.1. Study population

At the outset of the COVID-19 outbreak, the Italian National Institute of Health (Istituto Superiore di Sanità [ISS]) was in charge to establish the COVID-19 Integrated Surveillance System aimed at collecting data from all cases, including deaths, with SARS-CoV-2 infection throughout the country [14]. COVID-19-related deaths were

progressively spread out and influential voices have called for adequate attention to the impact of the COVID-19 crisis on the most vulnerable populations, including those with severe mental illness, learning difficulties, and neurodevelopmental disorders [2].

Psychiatric patients were found with more severe symptoms of depression and anxiety and more intense stress, insomnia, irritability

defined as those occurring in patients with positive RT-PCR for SARS-CoV-2, independently from pre-existing diseases that may have caused or contributed to death. A dedicated national surveillance on the characteristics of deceased SARS-CoV-2 positive patients covering all the Italian hospitals was put in place. As to COVID-19 related deaths, Italian Regions and Autonomous Provinces were asked to send ISS the medical charts of the hospitalisations during which the deaths occurred. A random sample of these clinical charts was selected to be representative (by gender, age, geographical distribution) of the concurrent distribution of the national deaths registered by the COVID-19 Integrated Surveillance System. The sampled clinical charts were reviewed by a group of medical doctors at the ISS (Protocol of the Italian surveillance on the characteristics of deceased SARS-CoV-2 positive patients, Supplementary Material).

As of 1st of September 2020, 35,957 COVID-19 related deaths occurred in Italy. The present cross-sectional study is based on the medical charts of 4020 COVID-19 related in-hospital deaths, that completed the ISS central review from February the 22nd 2020 to September the 1st 2020 representing 11.2% of all deaths occurred in Italy by that date. Sex, age and geographical distribution of sampled clinical charts and of overall in- and out-of-hospital deaths registered by the COVID-19 Integrated Surveillance System are shown in Tables 1 S-2 S (Supplementary Material).

2.2. Data collection and measures

Details on data and information collected from medical charts are given in the Supplementary Material. Information on previous comorbidities including PDs were self-reported, gathered from previous clinical documentation provided by the patient, or reported by the referring physician, and were identified from structured electronic health record diagnostic fields or unstructured text of the clinical chart. According to previous studies, patients were assigned to only one diagnostic category following the "hierarchy" of psychiatric diagnoses [16] by two experienced psychiatrists (EC, IL). The identified disorders were then assigned to two groups: (1) severe psychiatric disorders (SPDs), including schizophrenia and other psychotic disorders (corresponding to ICD10 diagnoses: F20-29) and bipolar and related disorders (ICD10 diagnoses: F30-F31); (2) common mental disorders (CMDs) [17], including depression without evidence of psychotic features (ICD10 diagnoses: F32-F34, F39) and anxiety disorders (ICD10:F40-F43). The adoption of two broad diagnostic categories aimed to reduce the potential misclassification bias related to the emergency non-psychiatric setting.

The transition of care of patients was evaluated in terms of days from symptoms' onset to: (i) hospital admission; (ii) pre-admission or in-hospital nasopharyngeal swab; (iii) intensive care unit (ICU) admission; and (iv) death. Shorter times between clinical onset, hospitalization, and death has been considered suggestive of a steeper clinical worsening, while longer time to testing and lower rate of admission in ICU of reduced access to care.

2.3. Statistical analysis

We reported frequency and prevalence for categorical variables and mean and 95% Confidence Intervals (CI) or median and Inter Quartile Range (IQR) for continuous variables, depending on data distribution.

Descriptive characteristics of patients dying with COVID-19 were reported by PD group (no PD, SPD, CMD). Median times of care transition were also reported by PD group.

In our sample of patients dying in hospital with COVID-19, Multinomial Logistic Regression models were implemented to assess the association of clinical characteristics and care pathways, as independent variables, with the PD handled, as dependent variable, in three categories (SPD, CMD, and no PD diagnosis). Crude Odds Ratios (OR)

with related 95% CI were estimated using single multinomial logistic regression models for each clinically relevant variable (age, sex, number of comorbidities, fever at admission, admission from LTCF, ICU admission, time from symptoms' onset to nasopharyngeal swab and hospital of death) with PD as the dependent variable. The variable 'Number of comorbidities', dichotomised in '0−2′ diseases and '3 and over' diseases categories, was included in the model instead of the single comorbidities to avoid multicollinearity and over-fitting effects. Adjusted Odds Ratios (aOR) and related 95% CI were estimated using a multinomial logistic regression model including the above mentioned clinically relevant variables and the hospital of death as independent variables, and PD as the dependent one.

Analyses were performed using IBM SPSS Statistics 26 for Windows.

3. Ethical approval

On February 27th, 2020, the Italian Presidency of the Council of Ministers established the COVID-19 Integrated Surveillance System surveillance and authorized scientific dissemination of anonymised data related to COVID-19 by the Italian Institute of Health (Civil Protection Department Decree n.640). Therefore, ethical approval and consent were not required.

4. Role of the funding source

There was no funding source for this study.

5. Results

The 4020 COVID-19 deaths included in the study took place in 365 hospitals across Italy. Based on the analysis of the 4020 medical charts of patients who have died in hospitals with confirmed COVID-19 between February 21st and August 3rd 2020 (reviewed by ISS until September the 1st), 261 patients (6.5%) had a previous psychiatric diagnosis. Of them, 84/4020 (2.1%) had an SPD (50 with schizophrenia or other psychotic disorder, 34 with bipolar or related disorder), 177/4020 (4.4%) had a CMD (105 with depressive disorder, 72 with anxiety disorder).

Table 1 summarizes demographic and clinical characteristics of the deceased patients at hospital admission, by presence/absence and type of previous psychiatric diagnosis. The mean age at death was 78.0 (95%CI 77.6−78.3) years among patients without a previous psychiatric diagnosis, 71.8 (95%CI 69.3−72.0) among those with an SPD, 79.5 (95%CI 78.0−81.1) among those with a CMD. 106 (59.9%) patients with a CMD were women, giving a female-to-male ratio of 1.5:1, while a ratio of 0.5:1 was observed in the other two groups of deceased patients. The burden of multi-morbidity was high in the whole sample, with 2455 (62.2%) deceased individuals suffering from three or more pre-existing comorbidities. 2253 (61.2%) individuals without a psychiatric diagnosis, 62 (73.8%) with an SPD, and 136 (78.2%) with a CMD were diagnosed with three or more comorbidities. By browsing the single disease hypertension and type 2 diabetes were the most frequent conditions in the group without a psychiatric diagnosis (2444 [66.4%]; 1109 [30.1%], respectively) and in the CMD group (113 [64.9%]; 47 [27.0%], respectively). Hypertension ranked also first in the SPD group (36 [42.9%]), followed by dementia (24 [28.6%]. Neurodevelopmental disorders were found among 43 (1.2%) deceased individuals with no PD, 10 (11.9%) with an SPD, and absent in the CMD group. Overall, 443 (11.8%) patients without a PD, 41 patients with an SPD (48.8%) and 54 with a CMD (30.5%) were admitted to hospital coming from LTCFs. These were non-psychiatric LTCFs in all cases, except for three patients with an SPD that came from psychiatric LTCFs.

Symptoms at admission, in-hospital complications and treatments among patients dying with COVID-19 according to psychiatric

Table 1
Age, sex, type and number of comorbidities in patients dying in hospital with COVID-19 according to psychiatric diagnosis.

	All (n = 4020)		No Psychiatric Disorder (n = 3759)		Severe Psychiatric Disorder (SPD) (n = 84)		Common Mental Disorder (CMD) (n = 177)	
Age (years)								
Mean (95%CI)	77.9 (77.5−78.3)		78.0 (77.6−78.3)		71.8 (69.3−72.0)		79.5 (78.0−81.1)	
Median (IQR)	80 (72−86)		80 (72−86)		72 (64−81)		82 (73−86)	
Sex								
Women (%)	1422 (35.4)		1287 (34.2)		29 (34.5)		106 (59.9)	
Men (%)	2598 (64.6)		2472 (65.8)		55 (65.5)		71 (40.1)	
Comorbidities	**n 3940**	**% 100.0**	**n 3682**	**% 93.5**	**n 84**	**% 2.1**	**n 174**	**% 4.4**
Hypertension	2596	65.8	2444	66.4	36	42.9	113	64.9
Type 2 diabetes	1173	29.7	1109	30.1	16	19.0	47	27.0
Ischemic heart disease	1092	27.7	1042	28.3	13	15.5	36	20.7
Atrial fibrillation	906	23.0	866	23.5	9	10.7	31	17.8
Chronic renal failure	806	20.4	763	20.7	11	13.1	31	17.8
Dementia	739	18.7	668	18.1	24	28.6	46	26.4
COPD	669	17.0	621	16.9	14	16.7	33	19.0
Active cancer	650	16.5	616	16.7	17	20.2	16	9.2
Heart failure	617	15.6	585	15.6	7	8.3	25	14.4
Obesity	423	10.7	390	10.6	8	9.5	24	13.8
Stroke	415	10.5	384	10.4	10	11.9	21	12.1
Respiratory failure	226	5.7	208	5.6	6	7.1	12	6.9
Chronic liver disease	173	4.4	162	4.4	4	4.8	6	3.4
Autoimmune disease	150	3.8	141	3.8	3	3.6	6	3.4
Dialysis	79	2.0	74	2.0	2	2.4	3	1.7
Neurodevelopmental disorders	54	1.4	43	1.2	10	11.9	0	0.0
HIV	7	0.2	7	0.2	0	0.0	0	0.0
N of comorbidities								
0	156	4.0	154	4.2	1	1.2	1	0.6
1	533	13.5	512	13.9	9	10.7	12	6.9
2	800	20.3	763	20.7	12	14.3	25	14.4
3 or more	2455	62.2	2253	61.2	62	73.8	136	78.2
Coming from LTCF	538	13.4	443	11.8	41	48.8	54	30.5

95% CI: 95% Confidence Interval; IQR: Interquartile range; COPD: Chronic obstructive pulmonary disease; LTCF: Long term care facility.

diagnosis are presented in Table 2. Fever and dyspnea were the most common symptoms at hospital admission in the three groups, being recorded in 2683 (73.9%) and 2678 (73.7%) individuals without PD, in 113 (64.9%) and 47 (27.0%) patients with an SPD, and in 110 (65.5%) and 123 (73.2%) cases of the CMD group. Acute respiratory distress syndrome was by far the most represented in-hospital complication, experienced by 3445 (95.6%) deceased individuals without a PD, 78 (96.3%) with an SPD, 168 (97.1%) with a CMD. Almost all patients received respiratory assistance: 3400 (94.2%) in the no PD group, 76 (93.8%) in the SPD and 164 (94.8%) in the CMD group. 778 (22.2%) individuals without a psychiatric diagnosis, 12 (15.6%) with an SPD and 24 (14.3%) with a CMD were admitted to ICU.

Times of care transitions are described in Table 3. Patients without PD were hospitalized and had SARS-CoV-2 test 4 days (IQR: 2−7) and 5 days (IQR: 3−9) after the onset of symptoms, respectively; death took place 6 days (IQR: 3−12) from hospitalization and 12 days (IQR: 8−19) after the onset of the disease. In the group of patients with SPD the median numbers of days from symptoms onset to hospital admission and to nasopharyngeal swab were 3 (IQR: 2−6) and 3 (IQR: 2−7), respectively; death occurred 8 days (IQR: 4−12) after hospital admission and 12 days (IQR: 6−21) from symptoms onset. In patients with CMD, 4 days (IQR: 2−9) was the median time from clinical onset to both hospitalization and SARS-CoV-2 testing. CMD patients died after 7 days (IQR: 3−14) from their hospital admission and 12 days (IQR: 7−22) after disease onset.

In Table 4 crude (ORs), adjusted (aORs) Odds Ratios, and relative 95%CI, are reported to evaluate the independent association of clinically relevant characteristics and care pathways with a prior

diagnosis of SPD or CMD in individuals who died with COVID-19. The adjusted multinomial logistic regression analysis included age, sex, number of comorbidities, admission from LTCF, ICU admission, time from symptoms' onset to nasopharyngeal swab, and hospital of death. The number of records having valid values for all the variables included in the model was 2760 (68.6%). Compared with dead patients without PD, those with SPD were younger (aOR for 1 year increment 0.96; 95% CI 0.94−0.98) and were more likely to be admitted from LTCF (aOR 9.02; 95% CI 4.99−16.30). Dead patients with CMD, as compared with those without PD, were more likely female (aOR 1.56; 95% CI 1.05−2.32) and were more frequently admitted from LTCF (aOR 2.09; 95% CI 1.19−3.66). When adjusted for the other variables, comorbidity burden, fever, admission to intensive care and time from symptoms' onset to nasopharyngeal swab and did not result significantly associated with an SPD or with a CMD in comparison to those without any PD.

6. Discussion

This is the first study describing characteristics, course, management, and care pathways of patients with a prior psychiatric diagnosis dying in hospital with COVID-19 compared to patients dying with COVID-19 and no previous psychiatric history.

Patients with SPDs, unlike patients with CMDs, were found to die with COVID-19 at a younger age than other individuals deceased in hospital without a prior psychiatric diagnosis. Nasopharyngeal swab and access to intensive care of critically ill COVID-19 patients were provided to patients with and without a psychiatric diagnosis

Table 2
Symptoms at admission, in-hospital complications and treatments among patients dying with COVID-19 according to psychiatric diagnosis.

	All (n = 4020)		No Psychiatric Disorder (n = 3759)		Severe Psychiatric Disorder (SPD) (n = 84)		Common Mental Disorder (CMD) (n = 177)	
	n	%	n	%	n	%	n	%
Symptoms at admission	**3883**	**100.0**	**3633**	**93.6**	**82**	**2.1**	**168**	**4.3**
Fever	2866	73.7	2683	73.9	71	86.6	110	65.5
Dyspnea	2864	73.7	2678	73.7	60	73.2	123	73.2
Cough	1443	37.1	1360	37.4	26	31.7	54	32.1
Diarrhea	227	5.8	214	5.9	3	3.7	10	6.0
Hemoptysis	22	0.6	21	0.6	0	0.0	1	0.6
In-hospital complications	**3857**	**100.0**	**3603**	**93.4**	**81**	**2.1**	**173**	**4.5**
Acute Respiratory Distress Syndrome	3694	95.7	3445	95.6	78	96.3	168	97.1
Acute renal failure	900	23.3	831	23.1	19	23.5	50	28.9
Acute cardiac injury	421	10.9	393	10.9	11	13.6	16	9.2
Superinfection	684	17.7	637	17.7	14	17.3	32	18.5
Shock	844	21.9	790	21.9	15	18.5	39	22.5
In-hospital COVID-19 pharmacological treatments	**3895**	**100.0**	**3643**	**93.5**	**80**	**2.1**	**172**	**4.4**
Antibiotics	3378	86.6	3151	86.5	68	85.0	155	90.1
Antivirals, including hydroxychloroquine	2331	59.8	2185	60.0	47	58.8	97	56.4
Steroids	1641	42.1	1539	42.2	29	33.3	73	42.4
Tocilizumab	161	4.6	154	4.7	2	2.9	5	3.2
Respiratory assistance *	**3640**	**94.2**	**3400**	**94.2**	**76**	**93.8**	**164**	**94.8**
Intensive Care Unit admission **	**814**	**21.7**	**778**	**22.2**	**12**	**15.6**	**24**	**14.3**

*Missing data = 157.
**Missing data = 264.

without disparity, even in the situation of limited resources that occurred in Italy during the first phase of the epidemic. Patients with a psychiatric diagnosis were more often admitted to hospital from a LTCF compared to patients without a psychiatric history.

Recent studies suggest that a psychiatric history might be an independent risk factor for COVID-19 infection and mortality [9–11]. Our study provides mental health professionals and policymakers with further information to be taken into consideration to protect health and do not harm people living with PDs in the pandemic scenario.

First, while the excess mortality in people with schizophrenia and bipolar disorder is widely acknowledged [18], we found people with an SPD dying at a younger age, also from COVID-19. Second, in accordance with the evidence that female sex is the most consistent risk factor for depression and many anxiety disorders [19], women were

Table 3
Transition of care among patients dying with COVID-19 according to psychiatric diagnosis.

	All (n = 4020)		No Psychiatric Disorder (n = 3759)		Severe Psychiatric Disorder (SPD) (n = 84)		Common Mental Disorder (CMD) (n = 177)	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Time (in days) from symptoms' onset to:								
Hospital admission	4	2–7	4	2–7	3	2–6	4	2–9
Nasopharyngeal swab	5	2–9	5	3–9	3	2–7	4	2–9
Death	12	7–19	12	8–19	12	6–21	12	7–22
Time (in days) from hospital admission to death	7	3–13	6	3–13	8	4–12	7	3–14

Table 4
Crude and adjusted multinomial logistic regression analysis of psychiatric disorders (severe or common versus no-psychiatric disorder) in individuals dying with COVID-19.

	Crude OR	95% CI	Adjusted OR*	95% CI
Severe psychiatric disorder (SPD)				
Older age (per 1 year increment)	0.97	0.95–0.98	0.96	0.94–0.98
Female vs male	1.01	0.64–1.60	1.10	0.64–1.87
N. of comorbidities (3 or more vs 0 to 2)	1.79	1.09–2.92	1.37	0.79–2.36
Fever (yes vs no)	2.29	1.21–4.33	1.45	0.73–2.90
Admitted from LTCF (yes vs no)	7.14	4.60–11.07	9.02	4.99–16.30
Intensive Care Unit admission (yes vs no)	0.65	0.35–1.21	0.70	0.34–1.46
Time (in days) from symptoms' onset to nasopharyngeal swab (per 1-day increment)	0.98	0.94–1.02	0.99	0.96–1.03
Common mental disorder (CMD)				
Older age (per 1 year increment)	1.00	0.99–1.02	1.00	0.98–1.02
Female vs male	2.87	2.11–3.90	1.56	1.05–2.32
N. of comorbidities (3 or more vs 0 to 2)	2.27	1.58–3.27	1.23	0.81–1.88
Fever (yes vs no)	0.67	0.48–0.93	0.94	0.60–1.48
Admitted from LTCF (yes vs no)	3.29	2.35–4.59	2.09	1.19–3.66
Intensive Care Unit admission (yes vs no)	0.59	0.38–0.91	0.87	0.49–1.54
Time (in days) from symptoms' onset to nasopharyngeal swab (per 1-day increment)	1.02	1.00–1.04	1.01	0.99–1.04

* Adjusted for the other variables in the table and the 'Hospital of death' variable.

overrepresented among individuals who died with COVID-19 and a CMD despite the well-known preponderance of men among individuals dying with COVID-19.

The prevalence of specific non-psychiatric comorbidities among patients with a severe psychiatric diagnosis in our study, was higher compared to those reported by the international literature (i.e., coronary heart disease, cerebrovascular disease, congestive heart failure pooled prevalence for SPDs: 9.9% [20]; type 2 diabetes prevalence in schizophrenia 13.7% and bipolar disorder 13.7%[21]. Patients with an SPD and those with a CMD in our sample were frequently affected by cognitive impairment in the form of dementia or intellectual disability. The association between PDs and a higher risk for late-life dementia is well recognized [22], and the overlap of previous PDs and dementia is common among elderly patients [23]. Likewise, concurrent PDs among adults with intellectual disability are commonly observed in the clinical practice [24]. Differently from the potential risks for poorer outcomes from COVID-19 among individuals with a severe mental illness that were envisaged [5], it was not the increased prevalence of cardiovascular, respiratory or metabolic disease to characterize this population in our study, but it was rather a general condition of vulnerability possibly related to the high overall comorbidity burden and to the high prevalence of cognitive impairment. This is in agreement with the finding that frailty increases risk of mortality, even after accounting for age and other known comorbidities linked to COVID-19 [25]. In this respect, some European countries are revising their vaccination strategy to include patients with severe mental illness among those with high priority for COVID-19 vaccination, and an appeal has recently been launched for other countries to follow this example [26].

The high percentage of patients with a PD hospitalised from non-psychiatric LTCFs should be a cause of concern and inform mental health professionals and policymakers of the urgent need to reconsider mental health care pathways. COVID-19-related deaths among LTCFs residents represented 30−60% of all COVID-19 deaths in several European countries [8], A dedicated survey monitoring the spread of SARS-CoV-2 infection in the Italian nursing homes, found confirmed cases of COVID-19 or influenza like-symptoms in 67.7% of the 1343 participating facilities [27], where the situation was dramatic [28]. Among the characteristics of patients deceased with COVID-19 with a psychiatric diagnosis described by our study, living in LTCFs outside the mental health service is the one on which we can, and must, act immediately.

Several examples of the Italian mental health service preparedness during the COVID-19 emergency have been described. In Lombardy, psychiatric wards have been organized with dedicated areas for COVID-19 positive patients with acute PDs and no severe medical symptoms [29]. The small size of the psychiatry wards and their location inside the general hospitals may have contributed to avoid the large clusters observed elsewhere [6]. The main organizational challenges occurred in community residential facilities, forced to raise barriers instead of breaking them down, where patients found themselves suddenly confined, with very limited or no leave and severe visitor restrictions [30]. Our study sheds light on the condition and on the need to protect the frailest and older patients with a psychiatric diagnosis that, due to the overwhelming physical comorbidities and the cognitive impairment, are spending their late life in non-psychiatric LTCFs. COVID-19 has the potential to put home− and community-based approach for people with mental health needs and general condition of fragility at the forefront, trying to reverse a trajectory of progressive loss of autonomy and combating at the same time the increased risk of social exclusion and infection related to long-term admissions in a residential setting.

A process aimed at reconverting residential care into personalised and socially inclusive home-based therapeutic rehabilitation care programmes has been underway for years in some Italian Regions [31]. Building on these experiences, a national decree calls for the need of urgently implementing innovative forms of integrated home-based assistance for people with chronic conditions, mental disorders and limited autonomy in response to COVID-19 emergency [32].

Our findings should be interpreted in light of several potential limitations. First, they focused on patients dying in hospital, while deaths occurring at home or in LTCFs were not included. Therefore, although our results represent the best evidence on COVID-19 related in-hospital mortality available in Italy to date, they are not representative of the national COVID-19 related deaths including in and out-of-hospital mortality. A second limitation arise from our reliance on medical charts compiled in situations of clinical urgency, with limited possibility of collecting detailed information on presence, severity and time of onset of comorbidities not directly connected with the admission. Less severe mental disorders are more likely not to be captured by routinely collected data [33]. In addition, when a factor of interest was not reported in the medical record, it was considered absent; therefore, it is possible that there was an underestimation of less visible and recognizable conditions. The prevalence of SPDs in our study population was consistent with the prevalence of 2.0% for psychotic disorders and of 1.2% for bipolar disorder resulting from the analysis of electronic health records of patients with COVID-19 infection in the USA [10,11]. The prevalence of CMDs in our study, though lower than those observed in the US [10,11], is consistent with reliable population-based national estimates [17]. Even if the presence of a mental disorder was missed in some cases, the effect of this misclassification would have been conservative, as it would have diluted the strength of the associations observed in the study. A further limitation is the poor reliability of the psychiatric diagnosis made by practicing clinicians without the support of semi-structured interviews. The accuracy of routinely collected mental health diagnosis data to a reference standard showed a positive predictive value above 80% for the broad category of "psychotic" illness, around 75% for unipolar depression and bipolar affective disorder and below 60% for anxiety disorders [33]. The adoption of two broad diagnostic categories is likely to have mitigated the impact of possible diagnostic errors (e.g., bipolar disorder misdiagnosed as schizophrenia, or panic disorder misdiagnosed as major depression). Moreover, some of the clinical characteristics explored by the study (i.e., comorbidity burden and time from symptoms' onset to nasopharyngeal swab among CMD; fever among SPD) did not result significantly associated with the psychiatric diagnosis after adjusting for the hospital of death. Lastly, the lack of a control group of individuals surviving to COVID-19 prevent us to identify any of the described characteristics as a risk factor for COVID-19 related death.

In conclusion, our study highlights the need of increasing mental health professionals and policymaker's awareness on the importance of protecting patients with an SPD from SARS-CoV-2 infection because they face COVID-19 dying to a younger age compared to patients without a PD, also in contexts where treatment is in place without disparity. Among actions that can be undertaken, the prioritization of patients with severe mental illness for COVID-19 vaccination should be considered. Concurrently, avoiding the inadequate residency of individuals with PDs in non-psychiatric LTCFs, and reconverting long-term non-rehabilitative residential care into personalised therapeutic rehabilitation projects are even more compelling in the present scenario.

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Contributors

IL, LN and EC conceived the study and interpreted the results. IL wrote the first draft of the manuscript. LP and GO substantially contributed to the interpretation of results. LP carried out data analysis and produced tables. IL, LN, LP, EC, NV, MLS, AP, AG, SB and GO reviewed and edited the manuscript. CLN and CD supervised data curation. LP, CLN, GO, IL and LN had full access to the database. All authors discussed the results, contributed to the final manuscript and approved the submitted version. The Members of the Italian National Institute of Health COVID-19 Mortality Group contributed to acquisition of data, data platform management, manuscript review, and approved the final version.

Data sharing statement

Because the data for study were sensible and not anonymised, they are not available for sharing.

Declaration of Competing Interest

Authors have no competing interest to disclose for the present study.

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Supplementary materials

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