September 22, 2021

Dr. Rochelle P. Walensky, Director
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30333

Dear Dr. Walensky,

As leading organizations dedicated to improving outcomes for people with mental health and substance use disorders, we write to ask you to add mental illnesses giving rise to increased risk of severe illness or death from COVID-19 to the CDC's list of medical conditions of heightened threat. Recent articles in *JAMA Psychiatry* (attached to this letter) as well as a lengthy body of research enumerated below confirm the additional risk from these conditions. The CDC has recently stated that "we anticipate an update to the information regarding mental illness will post in the coming weeks." We are grateful for the attention to the issue, however, given the grave implications for people with these conditions, we write to underscore the importance of moving forward and to request an immediate and urgent response.

International research, including two comprehensive meta-analyses, confirms that those with schizophrenia and other forms of serious mental illness are more at risk for severe illness and mortality from COVID-19. Other research demonstrates that a very modest effort to encourage vaccination leads to consistently higher rates of vaccination than that of the general population.[1] In short, guidance by the CDC directing public health officials to prioritize those with mental health conditions identified as high risk for severe illness or death due to COVID-19 will have a drastic impact on their survival rates, with only modest public investment needed.

We are also aware that communities are using the CDC medical condition list now to allocate scarce resources and the failure to include serious mental illness is having an immediate negative effect. For example, one community is using the list to prioritize access to shelter beds. (See the attached correspondence dated September 2 for an example of the adverse impact.) Many communities will use the list to target outreach, for eligibility to access booster shots, for services and housing, and other important benefits.

CDC guidance is routinely consulted by airlines, private companies, state and local government, schools and by individuals that rely on its expertise to make decisions on how to protect against infection. CDC often recommends that individuals in the high risk group take different actions to protect themselves from death or severe illness. Yet an individual with schizophrenia, identified as the highest risk group for death due to COVID-19 after the elderly in one study,

[1] Treatment Advocacy Center and Clubhouse International, *COVID-19 Vaccination for People with Severe Mental Illness: An International Survey,* September 15, 2021. Available online at: https://www.treatmentadvocacycenter.org/storage/documents/COVIDVaccine_FINAL.pdf

would not realize the need for additional protections for their own safety if they consulted the CDC's existing list. This is simply unacceptable.

President Biden has spoken at length of the need to prioritize those affected by mental health and substance use conditions during the pandemic. Officially designating mental illnesses that have been confirmed by research to carry a unique mortality risk during the pandemic for prioritization by the CDC is the only scientifically and morally defensible action to take and action should be taken quickly.

Our organizations hope that the CDC will seize this opportunity to demonstrate that individuals with these conditions are not invisible and deserve the consideration afforded to those living with other conditions appropriately identified on the CDC's list, including substance use disorders, despite a demonstrably lower mortality risk than for serious mental illnesses as identified in the attached research.

We have, by private letter and multiple public statements, made more than one urgent request to CDC on this issue. In the attached letter dated March 5, several organizations requested that these conditions be added to the list for prioritized response and we have recently contacted several CDC staff and appreciate their attention to the issue. We request, however, immediate and urgent action to add these conditions to the list given the negative, even deadly impact for individuals and communities and in view of the overwhelming evidence.

Sincerely,

American Foundation for Suicide Prevention
American Psychological Association
American Psychiatric Association
The Kennedy Forum
Massachusetts Association for Mental Health
Meadows Mental Health Policy Institute
Mental Health America
National Alliance on Mental Illness
National Association for Behavioral Healthcare
National Council for Mental Wellbeing
One Mind
Partner for Mental Health
Peg's Foundation
Steinberg Institute
Treatment Advocacy Center
Well Being Trust

cc: Assistant Secretary Miram E. Delphin-Rittmon (SAMHSA)
Sam Posner, Marie A. de Perio, John T. Brooks, Sapna Bamrah Morrs, Peter Briss (CDC)

American Foundation for Suicide Prevention

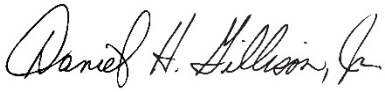
MAMH
Massachusetts Association for Mental Health

MEADOWS MENTAL HEALTH POLICY INSTITUTE

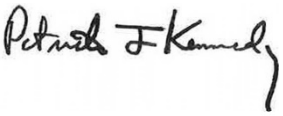
AMERICAN PSYCHIATRIC ASSOCIATION

Mental Health America

AMERICAN PSYCHOLOGICAL ASSOCIATION



National Alliance on Mental Illness



THE KENNEDY FORUM

National Association for Behavioral Healthcare

Access. Care. Recovery.

Peg's FOUNDATION

NATIONAL COUNCIL for Mental Wellbeing

HEALTHY MINDS • STRONG COMMUNITIES

STEINBERG INSTITUTE

ONE MIND

TREATMENT ADVOCACY CENTER

partner FOR MENTAL HEALTH

WELL BEING TRUST

Summary of evidence to inform the addition of serious mental illness as an underlying medical condition that increase a person's risk of severe illness or death from COVID-19

Systematic Review and Meta-analysis:

- Fond G, Nemani K, Etchecopar-Etchart D, et al. Association between mental health disorders and mortality among patients with COVID-19 in 7 countries: A systematic review and meta-analysis. *JAMA Psychiatry.* (2021) doi:10.1001/jamapsychiatry.2021.2274
- Ceban, F., Nogo, D., Carvalho, I.P., et al. Assocation between mood disorders and risk of COVID-19 infection, hospitalization, and death: A systematic review and meta-analysis. *JAMA Psychiatry.* (2021). Doi:10.1001/jamapsychiatry.2021.1818

Case-control:

- Ji W, Huh K, Kang M, Hong J, Bae GH, Lee R, et al. Effect of underlying comorbidities on the infection and severity of COVID-19 in Korea: a nationwide case-control study. *J Korean Med Sci*. (2020) 35:e237. doi: 10.3346/jkms.2020.35.e237
- Wang Q, Xu R, Volkow ND. Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States. *World Psychiatry*. (2020) 20:124–30. doi: 10.1002/wps.20806

Cohort:

- Nemani K, Li C, Olfson M, Blessing EM, Razavian N, Chen J, et al. Association of psychiatric disorders with mortality among patients with COVID-19. *JAMA Psychiatry*. (2021) 78:380–6. doi: 10.1001/jamapsychiatry.2020.4442
- Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. *Lancet Psychiatry*. (2020) 8:30–140. doi: 10.1016/S2215-0366(20)30462-4
- Fond G, Pauly V, Leone M, Llorca PM, Orleans V, Loundou A, et al. Disparities in intensive care unit admission and mortality among patients with schizophrenia and COVID-19: a national cohort study. *Schizophr Bull*. (2020) sbaa158. doi: 10.1093/schbul/sbaa158
- Wang Q, Xu R, Volkow ND. Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States. *World Psychiatry*. (2020) 20:124–30. doi: 10.1002/wps.20806
- Lee SW, Yang JM, Moon SY, Yoo IK, Ha EK, Kim SY, et al. Association between mental illness and COVID-19 susceptibility and clinical outcomes in South Korea: a nationwide cohort study. *Lancet Psychiatry*. (2020) 1025–31. doi: 10.1016/S2215-0366(20)30421-1
- Care Quality Commission. *COVID-19 Insight 5: Our Data: Care Quality Commission*. (2021). Available online at: https://www.cqc.org.uk/publications/major-reports/covid-19-insight-5-our-data
- Bitan D, Krieger I, Kridin K, et al. COVID-19 Prevalence and Mortality Among Schizophrenia Patients: A Large-Scale Retrospective Cohort Study. *Schizopr Bull.* (2021) doi:10.1093/schbul/sbab012

Other:

- Fond G, Pauly V, Leone M, Llorca PM, Orleans V, Loundou A, et al. Disparities in intensive care unit admission and mortality among patients with schizophrenia and COVID-19: a national cohort study. *Schizophr Bull*. (2020) sbaa158. doi: 10.1093/schbul/sbaa158

JAMA Psychiatry | Original Investigation

Association of Psychiatric Disorders With Mortality Among Patients With COVID-19

Katlyn Nemani, MD; Chenxiang Li, PhD; Mark Olfson, MD, MPH; Esther M. Blessing, MD, PhD; Narges Razavian, PhD; Ji Chen, MS; Eva Petkova, PhD; Donald C. Goff, MD

IMPORTANCE To date, the association of psychiatric diagnoses with mortality in patients infected with coronavirus disease 2019 (COVID-19) has not been evaluated.

OBJECTIVE To assess whether a diagnosis of a schizophrenia spectrum disorder, mood disorder, or anxiety disorder is associated with mortality in patients with COVID-19.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study assessed 7348 consecutive adult patients for 45 days following laboratory-confirmed COVID-19 between March 3 and May 31, 2020, in a large academic medical system in New York. The final date of follow-up was July 15, 2020. Patients without available medical records before testing were excluded.

EXPOSURES Patients were categorized based on the following *International Statistical Classification of Diseases, Tenth Revision, Clinical Modification* diagnoses before their testing date: (1) schizophrenia spectrum disorders, (2) mood disorders, and (3) anxiety disorders. Patients with these diagnoses were compared with a reference group without psychiatric disorders.

MAIN OUTCOMES AND MEASURES Mortality, defined as death or discharge to hospice within 45 days following a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test result.

RESULTS Of the 26 540 patients tested, 7348 tested positive for SARS-CoV-2 (mean [SD] age, 54 [18.6] years; 3891 [53.0%] women). Of eligible patients with positive test results, 75 patients (1.0%) had a history of a schizophrenia spectrum illness, 564 (7.7%) had a history of a mood disorder, and 360 (4.9%) had a history of an anxiety disorder. After adjusting for demographic and medical risk factors, a premorbid diagnosis of a schizophrenia spectrum disorder was significantly associated with mortality (odds ratio [OR], 2.67; 95% CI, 1.48-4.80). Diagnoses of mood disorders (OR, 1.14; 95% CI, 0.87-1.49) and anxiety disorders (OR, 0.96; 95% CI, 0.65-1.41) were not associated with mortality after adjustment. In comparison with other risk factors, a diagnosis of schizophrenia ranked behind only age in strength of an association with mortality.

CONCLUSIONS AND RELEVANCE In this cohort study of adults with SARS-CoV-2–positive test results in a large New York medical system, adults with a schizophrenia spectrum disorder diagnosis were associated with an increased risk for mortality, but those with mood and anxiety disorders were not associated with a risk of mortality. These results suggest that schizophrenia spectrum disorders may be a risk factor for mortality in patients with COVID-19.

Multimedia

Supplemental content

CME Quiz at jamacmelookup.com and CME Questions page 452

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Corresponding Author: Donald C. Goff, MD, Department of Psychiatry, New York University Langone Medical Center, One Park Avenue, New York, NY 10016 (donald.goff@nyulangone.org).

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The coronavirus disease 2019 (COVID-19) pandemic has created unprecedented challenges to the health care system globally. Identification of risk factors associated with poor outcomes is important to guide clinical decision-making, target enhanced protective measures, and allocate limited resources. Risk factors identified to date include older age, male sex, cardiovascular disease, and diabetes.[1-5] Differences in outcomes by socioeconomic status and race have also received attention,[5-7] highlighting the potential for the pandemic to deepen existing health inequalities. However, evidence evaluating psychiatric diagnoses as potential risk factors for severe or fatal COVID-19 is limited.

The increased incidence of COVID-19 among individuals with mental disorders has been reported in at least 2 nationwide cohort studies in the US,[8,9] with depression and schizophrenia associated with the highest infection risk in one sample.[8] This association may be attributable to socioeconomic and environmental factors that contribute to exposure (eg, crowded housing, institutional settings, and lack of personal protective equipment). Because outcomes may differ by diagnosis, it is important to determine which infected patients are at increased risk of adverse outcomes. In a US cohort study of 1685 hospitalized patients with COVID-19, those with any psychiatric disorder had an increased risk of death, but specific diagnoses were not examined.[10] A Korean study found similar rates of adverse clinical events between patients with COVID-19 who had any mental illness and matched controls, but a higher risk of adverse clinical outcomes in individuals with severe mental illness.[11] To our knowledge, the risk of mortality by psychiatric diagnosis has yet to be evaluated.

The present study evaluated the association between psychiatric disorders and mortality among adults with COVID-19. Psychiatric disorders were grouped into schizophrenia spectrum disorders, mood disorders, and anxiety disorders. Based on previous studies of all-cause mortality,[12] we hypothesized that the risk of mortality would be increased in all 3 psychiatric diagnostic groups and would be highest for patients with schizophrenia spectrum disorders, intermediate for mood disorders, and lowest in patients with anxiety disorders compared with patients without psychiatric diagnoses.

Key Points

Question Is a diagnosis of schizophrenia spectrum, mood, or anxiety disorders associated with increased risk of mortality in patients with coronavirus disease 2019 (COVID-19)?

Findings In this cohort study of 7348 adults with laboratory-confirmed COVID-19 in a New York health system, a schizophrenia spectrum diagnosis was associated with an increased risk of death after adjusting for demographic and medical risk factors. Mood and anxiety disorders were not associated with increased risk of mortality.

Meaning A diagnosis of a schizophrenia spectrum disorder may be a risk factor for mortality in patients with COVID-19.

Methods

Study Design and Population

This retrospective cohort study was performed at the New York University (NYU) Langone Health System. The study was approved by the institutional review board of the NYU Grossman School of Medicine with a waiver of authorization for informed consent based on the determination that there was no more than minimal risk to patients in this observational study. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

We identified consecutive adult patients, aged 18 years or older, with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test results recorded between March 3 and May 31, 2020, in the NYU Langone Health electronic health record system. The health system includes more than 260 outpatient office sites and 4 acute care hospitals in Manhattan, Brooklyn, and Long Island, New York. Testing included real-time reverse transcriptase–polymerase chain reaction assays of nasopharyngeal, oropharyngeal, and sputum samples. The results were classified as positive if any test result was positive for SARS-CoV-2 RNA or negative if all test results were negative. Patients without medical records of encounters before March 3, 2020, were excluded. To preserve confidentiality, patients whose documented sex was not male or female were also excluded. Clinical outcomes were monitored for 45 days following the index testing date.

Data Collection and Definitions

For all identified patients with SARS-CoV-2 test results, we extracted psychiatric diagnostic codes from their electronic health records using billing/encounter diagnoses, external claim diagnoses, and inpatient hospital problems before their testing encounter. Patients were categorized in a hierarchical fashion into 3 mutually exclusive psychiatric diagnostic categories on the basis of *International Statistical Classification of Diseases, Tenth Revision*, codes documented before March 3, 2020, and before COVID-19 testing: (1) schizophrenia spectrum disorders, (2) mood disorders, and (3) anxiety disorders (eTable 1 in the Supplement provides *ICD-10* codes). Patients in each category were compared with a reference group of all remaining patients without psychiatric diagnoses documented before March 3, 2020. The reference group excluded patients with other primary psychiatric disorders (eTable 1 in the Supplement), but patients with organic mental disorders (*ICD-10* codes F00-F09), mental disorders due to substance use (*ICD-10* codes F10-F19), mental retardation (*ICD-10* codes F70-79), and disorders of psychological development (*ICD-10* codes F80-F89) were included in the reference group.

Because *ICD-10* codes for schizophrenia spectrum disorders include nonspecific diagnostic codes (F23, acute and transient psychotic disorders; F29, unspecified nonorganic psychosis), medical records review was performed for all SARS-CoV-2–positive patients with schizophrenia spectrum disorders for diagnostic validity. Review was performed

blinded to outcome. Patients with psychosis secondary to a neurologic or medical condition were assigned to the reference group. Patients with clear documentation indicating the absence of a schizophrenia spectrum diagnosis and the presence of an alternative psychiatric diagnosis were assigned to the appropriate diagnostic group.

The primary analysis included all patients with a psychiatric diagnosis of interest documented in any encounter before March 3, 2020. A secondary analysis was limited to patients with recently documented psychiatric diagnoses of interest recorded in an encounter between January 1, 2019, and March 3, 2020 (recent diagnoses). The same reference group of patients without psychiatric illness was used in both analyses.

The following patient-level characteristics were considered potentially related to both diagnostic category and COVID-19 outcome: age, sex, race, hypertension, diabetes, myocardial infarction, heart failure, chronic obstructive pulmonary disease, chronic kidney disease, smoking status, and cancer. Race was determined by patient report (aggregated into Black, Asian, White, mixed, other, and unknown) and was included based on literature reporting differences in COVID-19-related mortality by race.[5-7] Medical comorbidities were extracted from encounters before March 3, 2020, and included diagnoses documented from the medical history, inpatient and outpatient problem list, billing/encounter and external claims, following previous reports.[2-4,13] Missing data for race and smoking status were assigned to unknown categories.

The outcome, mortality, was defined as death or discharge to hospice. Clinical outcomes were monitored for 45 days following testing and included data through July 15, 2020.

Statistical Analysis

The prevalence of psychiatric disorders among all patients tested for COVID-19 and among those who tested positive was first determined. Descriptive statistics were used to report the likelihood of a positive test result in each psychiatric diagnostic group compared with the reference group.

The 45-day mortality outcome was compared between each psychiatric diagnostic group and the reference group using odds ratios (ORs): odds (psychiatric group)/odds (reference group). Three types of ORs were estimated: (1) unadjusted; (2) demographically adjusted for sex, age (18-44, 45-54, 55-64, 65-74, and ≥75 years, with 18-44 years serving as the reference group), and race (Asian, Black, White, mixed, and other); and (3) fully adjusted for the demographic factors plus hypertension, diabetes, myocardial infarction, heart failure, chronic obstructive pulmonary disease, chronic kidney disease, smoking status, and cancer. Logistic regression models that included indicators for the psychiatric diagnostic categories (3 indicators with the control group as reference) were used to estimate ORs and the covariates were included to estimate the 3 types of ORs; 95% CIs were estimated based on those models. As a sensitivity analysis, for the fully adjusted ORs, a stepwise selection/elimination procedure was performed with candidate variable entry and exit criteria set to $P = .05$, with 2-tailed, unpaired testing. All analyses were conducted using SAS, version 9.3 (SAS Institute Inc).

Results

Patient Characteristics at Baseline

A total of 31 044 adult patients were tested for COVID-19 between March 3 and May 31, 2020. There were 2425 patients excluded owing to lack of diagnostic records before March 3, 2020; 2075 excluded owing to a primary psychiatric diagnosis that did not meet the criteria for schizophrenia spectrum, mood, or anxiety disorder categories (eTable 1 in the Supplement); and 4 patients excluded whose documented sex was not male or female. Of the remaining 26 540 patients tested, 7348 (27.7%) had a positive result (3891 [53.0%] women; 3457 [47.0%] men); mean (SD) age was 54 (18.6) years. Of eligible patients with positive test results, 75 patients (1.0%) had a history of a schizophrenia spectrum illness, 564 (7.7%) had a history of a mood disorder, and 360 (4.9%) had a history of an anxiety disorder. Baseline characteristics of the patients by group are reported in **Table 1**. The likelihood of a positive test among the diagnostic groups was 22.3% for the schizophrenia spectrum group, 25.4% for the mood disorder group, 24.1% for the anxiety disorder group, and 28.2% for the reference group (eTable 2 in the Supplement).

45-Day Mortality

Overall, 864 patients (11.8%) died or were discharged to hospice within 45 days of a positive SARS-CoV-2 test result. A schizophrenia spectrum diagnosis was significantly associated with 45-day mortality after adjustment for age, sex, and race (OR, 2.87; 95% CI, 1.62-5.08) and after additional adjustment for medical risk factors (OR, 2.67; 95% CI, 1.48-4.80). After demographic adjustment, mood disorder diagnoses (OR, 1.25; 95% CI, 0.98-1.61) and anxiety disorder diagnoses (OR, 0.97; 95% CI, 0.67-1.41) were not significantly associated with mortality (**Table 2**). **Table 3** reports risk factors associated with COVID-19 mortality ordered by the magnitude of ORs from the fully adjusted logistic regression model. Diagnoses of mood disorders (OR, 1.14; 95% CI, 0.87-1.49) and anxiety disorders (OR, 0.96; 95% CI, 0.65-1.41) were not associated with mortality after adjustment. Results from a sensitivity analysis with stepwise selection of variables yielded similar results (eTable 3 in the Supplement).

In the secondary analysis of patients with recently documented psychiatric diagnoses, a schizophrenia spectrum diagnosis was associated with 45-day mortality after adjustment for age, sex, and race (OR, 3.13; 95% CI, 1.50-6.54) and after additional adjustment for medical risk factors (OR, 2.67; 95% CI, 1.26-5.69). A mood disorder diagnosis was associated with mortality after adjustment for demographic variables (OR, 1.52; CI, 1.13-2.03), but the association was not significant after additional adjustment for medical risk factors (OR, 1.27; 95% CI, 0.94-1.73). Anxiety disorders were not associated with mortality after demographic (OR, 1.24; 95% CI, 0.80-1.93) or additional (OR, 1.21; 95% CI, 0.77-1.90) adjustment (**Table 4**). The relative ranking of ORs for 45-day mortality associated with psychiatric diagnoses compared with other risk factors is provided in **Table 5**. Results from a

Table 1. Baseline Characteristics of Patients With Positive SARS-CoV-2 Test Results

Characteristic	No. (%)			
	Schizophrenia spectrum (n = 75)	Mood disorders (n = 564)	Anxiety disorders (n = 360)	Reference group (n = 6349)
Sex				
Male	42 (56.0)	225 (39.9)	143 (39.7)	3047 (48.0)
Female	33 (44.0)	339 (60.1)	217 (60.3)	3302 (52.0)
Age, y				
Mean (SD)	59.7 (15.0)	62.3 (18.7)	54.9 (19.3)	53.6 (18.4)
18-44	13 (17.3)	107 (19.0)	118 (32.8)	2212 (34.8)
45-54	9 (12.0)	64 (11.4)	61 (16.9)	1084 (17.1)
55-64	17 (22.7)	109 (19.3)	65 (18.1)	1201 (18.9)
65-74	27 (36.0)	126 (22.3)	46 (12.8)	890 (14.0)
≥75	9 (12.0)	158 (28.0)	70 (19.4)	962 (15.2)
Race				
White	47 (62.7)	326 (57.8)	220 (61.1)	2428 (38.2)
Black	17 (22.7)	73 (12.9)	44 (12.2)	1182 (18.6)
Asian	0	13 (2.3)	9 (2.5)	496 (7.8)
Other[a]	8 (10.7)	115 (20.4)	66 (18.3)	1489 (23.5)
Mixed	3 (4.0)	12 (2.1)	9 (2.5)	175 (2.8)
Unknown	0	25 (4.4)	12 (3.3)	579 (9.1)
Smoking status				
Current	20 (26.8)	43 (7.6)	38 (10.6)	270 (4.3)
Former	11 (14.7)	181 (32.1)	95 (26.4)	1046 (16.5)
Never	39 (52.0)	327 (58.0)	220 (61.1)	3997 (63.0)
Unknown	5 (6.7)	13 (2.3)	7 (1.9)	1036 (16.3)
Hypertension	58 (77.3)	388 (68.8)	190 (52.8)	2701 (42.5)
Heart failure	18 (24.0)	121 (21.5)	44 (12.2)	338 (5.3)
Myocardial infarction	32 (42.7)	210 (37.2)	89 (24.7)	839 (13.2)
Diabetes	28 (37.3)	232 (41.1)	91 (25.3)	1542 (24.3)
Chronic kidney disease	12 (16.0)	140 (24.8)	52 (14.4)	524 (8.3)
COPD	39 (52.0)	270 (47.9)	135 (37.5)	1321 (20.8)
Cancer	21 (28.0)	270 (47.9)	158 (43.9)	1396 (22.0)

Abbreviations: COPD, chronic obstructive pulmonary disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Other race included Guamanian or Chamorro, Native American, other Pacific Islander, Native Hawaiian, Samoan, or unspecified other race by patient report.

sensitivity analysis with stepwise selection of variables yielded similar results (eTable 4 in the Supplement).

Discussion

In this retrospective cohort study of 7348 patients with confirmed COVID-19, a schizophrenia spectrum diagnosis was associated with increased odds for 45-day mortality after controlling for age, sex, race, and known medical risk factors. Without adjustment, the odds for mortality in adults with mood disorders was increased compared with the reference group but was no longer statistically significant after adjustment for demographic characteristics and medical comorbidities. There was not a significant association between an anxiety disorder diagnosis and mortality.

Although previous observational studies in the US have reported an increased incidence of COVID-19 among patients with psychiatric disorders[8,9] and increased mortality risk in broadly defined cohorts of patients with any mental disorder,[8,10] to our knowledge, this is the first study to report the risk of mortality by psychiatric diagnostic group. The results of this analysis suggest that the risk of severe or fatal illness may differ by diagnosis. In a population that may be more susceptible to infection, determining which patients may be at highest risk for adverse outcomes is necessary to guide clinical decision-making, including the need for enhanced monitoring and targeted interventions.

The results should be interpreted with several caveats. During the study period, the pandemic was at its peak in New York City. Testing was largely restricted to symptomatic and high-risk people, as reflected in the high rate of positive test results (27.7%). The study population was limited to patients who had access to treatment within the NYU health care system and received testing and evaluation. Mortality risk was increased in those with recent documentation of a mood disorder after demographic adjustment, suggesting that stage of illness (acute vs stable) may contribute to differential risk in patients with episodic psychiatric disorders.

The most notable finding from this study is the high risk of mortality associated with schizophrenia spectrum diagnoses, ranking second behind age in strength of an association

Table 2. Odds Ratios and Rates of 45-Day Case Fatality by Lifetime Psychiatric Diagnosis

SARS-CoV-2– Positive	Mortality or hospice, No. (%)	OR (95% CI)		
		Unadjusted	Demographically adjusted[a]	Fully adjusted[b]
All patients (n = 7348)	864 (11.8)	NA	NA	NA
Schizophrenia spectrum (n = 75)	20 (26.7)	2.93 (1.75, 4.92)	2.87 (1.62-5.08)	2.67 (1.48-4.80)
Mood disorders (n = 564)	104 (18.4)	1.82 (1.45, 2.29)	1.25 (0.98-1.61)	1.14 (0.87-1.49)
Anxiety disorders (n = 360)	39 (10.8)	0.98 (0.70, 1.38)	0.97 (0.67-1.41)	0.96 (0.65-1.40)
Reference[c] (n = 6349)	701 (11.0)	1 [Reference]	1 [Reference]	1 [Reference]

Abbreviations: NA, not applicable; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] The demographically adjusted OR included age, race, and sex.

[b] The fully adjusted model included demographic variables in addition to smoking status, hypertension, heart failure, myocardial infarction, diabetes, chronic kidney disease, chronic obstructive pulmonary disease, and cancer.

[c] The reference group excluded patients with any history of a schizophrenia spectrum, mood, or anxiety disorder diagnosis or other psychiatric diagnoses listed in eTable 1 of the Supplement.

Table 3. Multivariable-Adjusted Risk Model for 45-Day Case Fatality, With Lifetime Psychiatric Diagnoses[a]

Variable	OR (95% CI)
Age, y	
18-44	1 [Reference]
≥75	35.72 (22.99-55.52)
65-74	16.54 (10.60-25.82)
55-64	7.74 (4.95-12.10)
45-54	3.89 (2.40-6.30)
Schizophrenia spectrum disorder	2.67 (1.48-4.80)
Male sex	1.69 (1.43-2.00)
Heart failure	1.60 (1.24-2.06)
Other race vs White race[b]	1.47 (1.19-1.80)
White race vs Black race	1.41 (1.10-1.81)
Hypertension	1.38 (1.12-1.70)
Asian race vs White race	1.28 (0.94-1.75)
Diabetes	1.27 (1.07-1.51)
Never smoker vs current smoker	1.27 (0.84,1.93)
Chronic kidney disease	1.23 (0.98-1.55)
Mood disorder diagnosis	1.14 (0.87-1.49)
White race vs mixed race	1.08 (0.60-1.97)
Cancer	1.01 (0.85-1.22)
Former smoker vs never smoker	1.00 (0.93-1.22)
Myocardial infarction	1.00 (0.81-1.22)
Anxiety disorder	0.96 (0.65-1.41)
Chronic obstructive pulmonary disease	0.93 (0.77-1.12)

Abbreviation: OR, odds ratio.

[a] Excluding unknown race and unknown smoking history.

[b] Other race included Guamanian or Chamorro, Native American, other Pacific Islander, Native Hawaiian, Samoan, or unspecified other race by patient report.

among all demographic and medical risk factors examined in this sample. Individuals with schizophrenia spectrum disorders had 2.7 times the odds of dying after adjustment for known risk factors. A higher risk with schizophrenia spectrum diagnoses was expected based on previous studies of all-cause mortality, but the magnitude of the increase after adjusting for comorbid medical risk factors was unexpected. It is possible that unmeasured medical comorbidities contributed to this finding, although the risk remained significantly increased after adjustment for multiple established risk factors. Delays in treatment seeking or reduced access to care may have contributed to worse outcomes. However, the lower rate of positive test results in the schizophrenia spectrum group compared with the reference group argues against selection bias as an explanation for the higher odds of mortality observed.

Beyond systemic barriers to care and delayed treatment, adults with schizophrenia spectrum diagnoses may be more susceptible to COVID-19 mortality due to biological factors related to their psychiatric illness or treatment. The results of this analysis are consistent with those of a nationwide study from South Korea in which government-mandated testing and enhanced monitoring were provided to all citizens. The investigators reported a similar risk of infection but higher risk of severe clinical outcomes in patients with psychotic disorders.[11] Although the mechanism underlying this association is not clear, immune dysregulation in the setting of genetic or acquired risk factors is a possibility. Variation in the major histocompatibility complex is one of the most highly replicated findings in genome-wide association studies of schizophrenia susceptibility,[14-17] and previous research has shown deficits in cellular immunity resulting in dysfunctional T cell–mediated immune responses in patients with schizophrenia.[18,19] Genetic variability across major histocompatibility complex class I genes may contribute to differences in immune response to COVID-19,[20] and inappropriate T-cell responses have been implicated in the pathophysiologic characteristics of severe infection.[21-23] Perturbations in inflammatory cytokine signaling have been reported in association with schizophrenia,[24-26] which may increase COVID-19 severity and mortality.[27]

Strengths and Limitations

This study has several strengths. Comprehensive data were collected from a large number of consecutive patients with laboratory-confirmed COVID-19. Focusing on patients with confirmed infection eliminated variability associated with differing rates of infection, which may differ between patients with and without psychiatric diagnoses. The cohort included a demographically diverse population of patients from across several sites in a health care system.

Table 4. Odds and Rates of 45-Day Case Fatality by Recent Psychiatric Diagnosis

SARS-CoV-2–Positive	Mortality or hospice, No. (%)	OR (95% CI)		
		Unadjusted	Demographically adjusted[a]	Fully adjusted[b]
All patients (n = 7003)	822 (11.7)			
Schizophrenia spectrum (n = 46)	12 (26.1)	2.84 (1.47-5.52)	3.13 (1.50-6.54)	2.67 (1.26-5.69)
Mood disorders (n = 374)	80 (21.4)	2.19 (1.69-2.84)	1.52 (1.13-2.03)	1.27 (0.94-1.73)
Anxiety disorders (n = 234)	29 (12.4)	1.14 (0.77-1.70)	1.24 (0.80-1.93)	1.21 (0.77-1.90)
Reference[c] (n = 6349)	701 (11.0)	1 [Reference]	1 [Reference]	1 [Reference]

Abbreviations: OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] The demographically adjusted OR included age, race, and sex.

[b] The fully adjusted model included demographic variables in addition to smoking status, hypertension, heart failure, myocardial infarction, diabetes, chronic kidney disease, chronic obstructive pulmonary disease, and cancer.

[c] The reference group excluded patients without any history of a schizophrenia spectrum, mood, or anxiety disorder diagnosis or other psychiatric diagnoses listed in eTable 1 of the Supplement.

The prevalence of psychiatric diagnoses in patients tested for COVID-19 was consistent with what would be expected based on nationwide prevalence.[28] Allowing 45 days for follow-up ensured that most patients had reached a primary outcome by the end of the study. By limiting the extraction of psychiatric history to encounters before March 3, 2020, we were able to determine the risk of critical illness and mortality associated with premorbid psychiatric illness rather than psychological sequelae of the virus or psychosocial stressors associated with the pandemic.

The study also has several limitations. First, the accuracy of clinical psychiatric diagnoses could not be validated in all patients. Psychiatric disorders were grouped into broad categories to maximize the sample size; there may have been differences in risk associated with specific diagnoses within categories. Second, individuals with psychiatric disorders may be less likely to seek medical attention owing to amotivation, social isolation, or stigma, particularly when there are systemic barriers to accessing care. However, all patients in this study had received previous treatment within the NYU Langone Health Network and access to care was previously established. Third, the generalizability of these findings to other patient populations and health care systems is uncertain. This study took place in a severely challenged health system during a peak of the COVID-19 pandemic. In addition, psychotropic medications used at the time of the infection were not assessed and may have been associated with either harmful or protective effects.

Table 5. Multivariable-Adjusted Risk Model for 45-Day Case Fatality, With Recent Psychiatric Diagnoses[a]

Variable	OR (95% CI)
Age, y	
18-44	1 [Reference]
≥75	35.70 (22.73-56.07)
65-74	16.60 (10.53-26.17)
55-64	7.75 (4.91-12.24)
45-54	3.90 (2.39-6.38)
Schizophrenia spectrum disorder	2.67 (1.26-5.69)
Male sex	1.74 (1.46-2.06)
Heart failure	1.65 (1.27-2.14)
Other race vs White race[b]	1.49 (1.21-1.85)
Hypertension	1.43 (1.15-1.77)
White race vs Black race	1.35 (1.05-1.75)
Never smoker vs current smoker	1.31 (0.84-2.04)
Asian race vs White race	1.29 (0.94-1.78)
Diabetes	1.28 (1.07-1.53)
Mood disorder diagnosis	1.27 (0.94-1.73)
Chronic kidney disease	1.21 (0.96-1.53)
Anxiety disorder diagnosis	1.21 (0.77-1.90)
Never smoker vs former smoker	1.02 (0.84-1.25)
Cancer	1.01 (0.83-1.21)
Myocardial infarction	1.01 (0.81-1.24)
Mixed race vs White race	1.01 (0.56-1.83)
Obstructive lung disease	0.97 (0.80-1.18)

Abbreviation: OR, odds ratio.

[a] Excluding unknown race and unknown smoking history.

[b] Other race included Guamanian or Chamorro, Native American, other Pacific Islander, Native Hawaiian, Samoan, or unspecified other race by patient report.

Conclusions

In this cohort study of adults with SARS-CoV-2–positive test results in a large medical system in New York, adults with schizophrenia spectrum diagnoses were at significantly increased risk of mortality after controlling for demographic and medical risk factors. The risk of mortality was increased in patients with recent documentation of a mood disorder after adjustment for demographic variables, but the association did not remain significant after adjustment for medical risk factors. There was no significant association between a diagnosis of anxiety disorder and mortality. To our knowledge, this is the first study to evaluate specific psychiatric disorders as independent risk factors for mortality in patients with COVID-19. Further research is needed to determine whether specific psychiatric disorders are associated with an increased risk of fatal illness among patients with COVID-19 in other settings. Targeted interventions may be needed for patients with severe mental illness to prevent worsening health disparities.

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JAMA Psychiatry | Original Investigation

Association Between Mental Health Disorders and Mortality Among Patients With COVID-19 in 7 Countries
A Systematic Review and Meta-analysis

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IMPORTANCE Heterogeneous evidence exists for the association between COVID-19 and the clinical outcomes of patients with mental health disorders. It remains unknown whether patients with COVID-19 and mental health disorders are at increased risk of mortality and should thus be targeted as a high-risk population for severe forms of COVID-19.

OBJECTIVE To determine whether patients with mental health disorders were at increased risk of COVID-19 mortality compared with patients without mental health disorders.

DATA SOURCES For this systematic review and meta-analysis, MEDLINE, Web of Science, and Google Scholar were searched from inception to February 12, 2021. Bibliographies were also searched, and the corresponding authors were directly contacted. The search paradigm was based on the following combination: (mental, major[MeSH terms]) AND (COVID-19 mortality[MeSH terms]). To ensure exhaustivity, the term *mental* was replaced by *psychiatric*, *schizophrenia*, *psychotic*, *bipolar disorder*, *mood disorders*, *major depressive disorder*, *anxiety disorder*, *personality disorder*, *eating disorder*, *alcohol abuse*, *alcohol misuse*, *substance abuse*, and *substance misuse*.

STUDY SELECTION Eligible studies were population-based cohort studies of all patients with identified COVID-19 exploring the association between mental health disorders and mortality.

DATA EXTRACTION AND SYNTHESIS Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline was used for abstracting data and assessing data quality and validity. This systematic review is registered with PROSPERO.

MAIN OUTCOMES AND MEASURES Pooled crude and adjusted odds ratios (ORs) for the association of mental health disorders with mortality were calculated using a 3-level random-effects (study/country) approach with a hierarchical structure to assess effect size dependency.

RESULTS In total, 16 population-based cohort studies (data from medico-administrative health or electronic/medical records databases) across 7 countries (1 from Denmark, 2 from France, 1 from Israel, 3 from South Korea, 1 from Spain, 1 from the UK, and 7 from the US) and 19 086 patients with mental health disorders were included. The studies covered December 2019 to July 2020, were of good quality, and no publication bias was identified. COVID-19 mortality was associated with an increased risk among patients with mental health disorders compared with patients without mental health disorders according to both pooled crude OR (1.75 [95% CI, 1.40-2.20]; $P<.05$) and adjusted OR (1.38 [95% CI, 1.15-1.65]; $P<.05$). The patients with severe mental health disorders had the highest ORs for risk of mortality (crude OR: 2.26 [95% CI, 1.18-4.31]; adjusted OR: 1.67 [95% CI, 1.02-2.73]).

CONCLUSIONS AND RELEVANCE In this systematic review and meta-analysis of 16 observational studies in 7 countries, mental health disorders were associated with increased COVID-19–related mortality. Thus, patients with mental health disorders should have been targeted as a high-risk population for severe forms of COVID-19, requiring enhanced preventive and disease management strategies. Future studies should more accurately evaluate the risk for patients with each mental health disorder. However, the highest risk seemed to be found in studies including individuals with schizophrenia and/or bipolar disorders.

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Supplemental content

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More than 100 million people have been infected with SARS-CoV-2, and almost 2.5 million have died of COVID-19 worldwide.[1] These numbers probably underestimate COVID-19 deaths by 50% owing to misclassified dementia and cardiovascular or metabolic deaths.[2] Patients with mental health disorders may be at particular risk of poor COVID-19 outcomes. Patients with mental health disorders can have multiple comorbidities that have been identified as risk factors for severe COVID-19: diabetes, hypertension, chronic obstructive respiratory disease, and end-stage kidney disease.[3] Mental health disorders are also associated with socioeconomic deprivation[4] and reduced access to care,[5] 2 important factors of poor COVID-19 outcomes.[6]

Data on the risks of poor COVID-19 outcomes among patients with mental health disorders continue to evolve from the first reports. Several population-based studies from South Korea, the US, and France revealed that severe mental health disorders (defined across studies by schizophrenia spectrum disorders and/or bipolar disorders) are risk factors for increased COVID-19 mortality.[7-9] The results were less clear for other mental health disorders (ie, depressive disorders, anxiety disorders, eating disorders, and personality disorders).[8-11] Determining whether patients with mental health disorders are at high risk of severe COVID-19 is an urgent research priority and can alert health policy makers and lead to adaptions in preventive care and disease management strategies to meet their health needs.[12] A preliminary meta-analysis has concluded that patients with mental health disorders were at increased risk of COVID-19 mortality.[13] However, this meta-analysis had methodological issues because the interdependency of effect sizes was not handled, in particular within each country. Moreover, mental health disorders were not analyzed separately, and there may be important discrepancies between diagnoses, which should guide health strategy priorities.

We carried out a systematic review and meta-analysis to synthesize the accumulating research on mental health disorders and COVID-19. The primary objective was to determine whether patients with mental health disorders are at increased risk of COVID-19 mortality compared with patients without mental health disorders. The secondary objectives were to determine whether patients with mental health disorders are at increased risk of intensive care unit (ICU) admission and which specific mental health disorders were associated with the risk of COVID-19 mortality.

Key Points

Question Is there a significant association between mental health disorders and COVID-19–related mortality?

Findings In this systematic review and meta-analysis of 16 observational studies in 7 countries with 19 086 patients, mental health disorders were associated with increased COVID-19 mortality according to both pooled crude and adjusted odds ratios. Patients with severe mental health disorders had the highest odds ratios.

Meaning These findings suggest that patients with COVID-19 and mental health disorders should be targeted as a high-risk population for severe forms of COVID-19, requiring enhanced preventive and disease management strategies.

Methods

Literature Search Strategy

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline.[14] Systematic bibliographic searches were carried out according to the Cochrane methodology. This project was registered in PROSPERO (CRD42021238038).

The search paradigm was based on the PubMed interface (MEDLINE database) and adapted for 2 databases: ScienceDirect and Google Scholar. The search paradigm was based on the following combination: (mental, major[MeSH terms]) AND (COVID-19 mortality[MeSH terms]). To ensure exhaustivity, the term *mental* was replaced by *psychiatric*, *schizophrenia*, *psychotic*, *bipolar disorder*, *mood disorders*, *major depressive disorder*, *anxiety disorder*, *personality disorder*, *eating disorder*, *alcohol abuse*, *alcohol misuse*, *substance abuse*, and *substance misuse*.

The last search was carried out on February 22, 2021. The reference lists and bibliographies of relevant reviews and articles retrieved from the database searches were manually searched for additional eligible articles. The authors of the relevant studies were contacted when additional data or clarifications were required.

Eligibility

The inclusion criteria were as follows: (1) articles in any language and with any date of publication; (2) original research articles; (3) population-based studies based on medico-administrative health databases or a health care data warehouse; (4) studies that included participants with a diagnosis of mental health disorders according to the *DSM* or any version of the *International Classification of Diseases (ICD)*; (5) studies on patients with clinical or biological diagnosis of COVID-19; and (6) articles with mortality and ICU admission data.

The titles and abstracts were screened by 2 researchers (G.F. and D.E.-E.). The full texts of the articles were then reviewed to determine whether they would be included by authors (G.F., D.E.-E., and L.B.).

Data Extraction

The following data were extracted: first author, timing (period of inclusion of cases and follow-up), databases, population, study setting, COVID-19 criteria inclusion, mental health disorders group definition, mean age, percentage of men, mortality rate, mortality crude odds ratio (OR), mortality adjusted OR, ICU admission crude OR, and ICU admission adjusted OR.

Two researchers (G.F. and D.E.-E.) extracted data from the included studies systematically using a predesigned extraction form. Each discrepancy in data extraction was examined by the first and last authors (G.F. and L.B.) to reach a consensus.

Assessment of Risk of Bias

To assess the risk of bias, we used the Newcastle-Ottawa Quality Assessment Scale. A good quality score required 3 or 4 stars for the selected item, 1 or 2 stars for the comparability item, and 2 or 3 stars for the outcomes item. A fair quality score required 2 stars for selection, 1 or 2 stars for comparability, and 2 or 3 stars for outcomes. A poor quality score required 0 or 1 star(s) for the selection, 0 stars for comparability, or 0 or 1 star(s) for outcome.

Statistical Analyses

A random-effects model was used to calculate the pooled crude and adjusted log ORs with 95% CIs for mortality and ICU admission. When available, we used the numbers of events and the sample sizes instead of the value of the crude ORs.[15] Because studies may show a certain degree of overlap in observations (several ORs per study and a potential higher-level unit by country), we used a 3-level random-effects (study/country) approach with a hierarchical structure.

We also investigated sources of heterogeneity using Cochran *Q* and I^2 statistics. I^2 is reported as a percentage out of 100%, whereby 0% to 40% denotes that the heterogeneity might not be important, 30% to 60% indicates moderate heterogeneity, 50% to 90% represents to substantial heterogeneity, and 75% to 100% indicates considerable heterogeneity.[16] Publication bias was assessed graphically with a funnel plot and statistically with modified Egger regression test computed by including the standard error as a predictor of effect sizes in the multilevel model.[17]

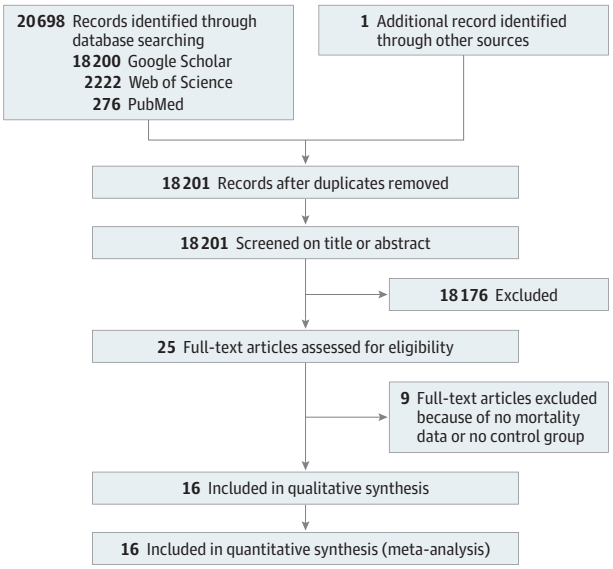
For subgroup analyses, we explored the association of the following study characteristics with outcomes: mean age older than 65 years vs 65 years and younger; inpatients and outpatients vs only inpatients; laboratory-confirmed COVID-19 vs *ICD* criteria inclusion; and severe mental health disorders (defined as schizophrenia spectrum disorder ± bipolar disorders if bipolar disorders were distinguished from other mood disorders) vs nonsevere mental health disorders (defined as mood disorders, anxiety disorders, personality disorders, eating disorders, and alcohol and substance misuses). All analyses were performed in R using the metafor package.[18] Two-sided *P* values were significant at .05.

Results

Search Strategy

We identified 18200 studies from the database search and no additional records through other sources. Sixteen studies met the eligibility criteria[7-11,19-27] (1 unpublished study by G.F. et al based on the French national hospital database) and were included in the quantitative analysis (**Figure 1**). A Swedish study[28] was not included because no data on patients with COVID-19 were available at the time of the analyses of the present work. Overall, the data of 19 086 patients with mental health disorders and COVID-19 were analyzed. It was not possible to determine the total number of individual patients, as some studies had overlaps in their samples.

Figure 1. Flowchart



Study Characteristics

The study and patient characteristics are presented in **Table 1** and **Table 2**. One study was carried out in Denmark,[24] 2 in France (including the unpublished study by G.F. et al),[7] 1 in Israel,[26] 3 in South Korea,[9-11] 1 in Spain,[19] 1 in the UK,[24] and 7 in the US.[8,20-23,27,29] The definition of the mental health disorders group varied across countries. The 3 South Korean studies,[9-11] 2 US studies,[21,27] and the UK study[25] included a large definition of mental health disorders (almost all F00-F90 codes) with addictions mixed with mental health disorders. Two US studies[22,23] included only patients with addictions (with no information on their mental status), and the Danish study[24] analyzed addictions separately from mental health disorders. No study reported on patients with the combination of a mental health disorder and addiction. It was possible to distinguish severe mental health disorders (as defined in the Methods section) in 6 studies (including the unpublished study by G.F. et al).[7-9,24,26] Only patients with schizophrenia were analyzed in the French and Israeli studies,[7,26] and patients with schizophrenia were included in a schizophrenia spectrum diagnosis group in 3 studies[8,9,26] and were combined with patients with bipolar disorders in 1 study.[24] Patients with bipolar disorders were analyzed separately in only 1 unpublished study by G.F. et al, and were included in the mood disorder group in 2 studies.[8,19] The last study, published as a letter, did not describe the mental health disorders of the patients in the mental health disorders group.[20]

Quality assessment

The study quality is presented in eTable 1 in the Supplement. All studies had a good quality score.

Meta-analysis

The forest plots of the adjusted ORs are presented in **Figure 2** (mental health disorders) and **Figure 3** (severe mental health

Table 1. Study Characteristics

Source	Timing	Database	Population	Study setting	COVID-19 criteria inclusion	Mental health disorders group definition
Denmark						
Reilev et al,[24] 2020	February 27 to May 19, 2020	Danish Microbiology Database linked to the Danish administrative and health care registries	Whole Danish population tested for SARS-CoV-2 infection	Inpatients and outpatients	Positive reverse transcription–polymerase chain reaction test	Mental health disorders (including schizophrenia and bipolar disorders); alcohol misuse; substance use
France						
Fond et al,[7] 2021	February 1 to June 9, 2020	French national hospital database for acute care	Whole French population hospitalized for COVID-19 aged ≥15 y	Inpatients	COVID-19 *ICD-10* codes (U07.1 or U07.2), respiratory symptoms (U07.10 or U07.11), and a length of hospital stay >24 h	Schizophrenia
Unpublished study by Fond et al	February 1 to June 9, 2020	French national hospital database for acute care. In this unpublished study, data were anonymized and can be reused for research purposes. No informed consent was necessary because all data were anonymous. This study was declared to the French National Data Protection Commission in accordance with the methodological reference MR005 (declaration number: 2203797).	Whole French population hospitalized for COVID-19 aged ≥15 y	Inpatients	COVID-19 *ICD-10* codes (U07.1 or U07.2), respiratory symptoms (U07.10 or U07.11), and a length of hospital stay >24 h	Bipolar disorders
Israel						
Tzur Bitan et al,[26] 2021	NA	Israeli health care database	5 Million citizens (half of the population)	Inpatients and outpatients	Positive reverse transcription–polymerase chain reaction test	Schizophrenia
South Korea						
Lee et al,[9] 2020	January 1 to May 15, 2020	South Korean national health insurance claims database	98% Of the whole population aged >20 y	Inpatients and outpatients	Positive reverse transcription–polymerase chain reaction test	One of the following mental health disorders: nonaffective psychotic disorders; affective psychotic disorders; anxiety- and stress-related disorders; alcohol or drug misuse; mood disorders without psychotic symptoms; eating disorders and personality disorders
Lee et al,[11] 2020	January 1 to April 10, 2020	South Korean National Health Insurance Review and Assessment Service database	Individuals aged ≥65 y	Inpatients and outpatients	Laboratory-confirmed COVID-19	Schizophrenia, psychotic disorders; bipolar disorders; depressive disorder; anxiety disorder; panic disorder, acute stress disorder; insomnia; dementia; organic mental disorder; psychoactive substance dependence; psychoactive substance use disorder; psychoactive substance-induced organic mental disorder; psychosomatic factor in physical condition
Jeon et al,[10] 2021	December 1, 2019, to May 15, 2020	South Korean national health insurance claims database linked to the Korea Disease Control and Prevention Agency database	Whole population without age restriction	Inpatients and outpatients	Diagnostic code (specific to the database)	Mental health disorders (included schizophrenia spectrum disorder and mood disorders)
Spain						
Poblador-Plou et al,[19] 2020	March 4 to May 17, 2020	PRECOVID database (created to follow patients with positive COVID-19 test results) linked to Aragon Health System	Spanish region of Aragon	Inpatients and outpatients	Laboratory-confirmed COVID-19	Bipolar disorders; depressive disorders; anxiety disorders
United Kingdom						
Yang et al,[25] 2020	January 31 to May 31, 2020	The UK Biobank	502 507 Participants, aged 40 to 69 y, from England, Scotland, and Wales	Inpatients	Positive reverse transcription–polymerase chain reaction test	Psychotic disorders; depressive disorders; anxiety; stress-related disorder; alcohol and substance misuse

(continued)

Table 1. Study Characteristics (continued)

Source	Timing	Database	Population	Study setting	COVID-19 criteria inclusion	Mental health disorders group definition
United States						
Allen et al,[22] 2020	January 1 to October 26, 2020	NYULH linked to NYULH's COVID-19 deidentified clinical database, which includes data from 4 acute care hospitals	Individuals in greater New York City	Inpatients and outpatients	Positive reverse transcription-polymerase chain reaction test	Any alcohol or substance use disorder excluding nicotine dependence
Baillargeon et al,[23] 2021	February 20 to July 31, 2020	TriNetX Research Network platform database, which includes data from 35 health care organizations including hospitals, primary care clinics, and specialty treatment institutions	Approximately 54 million patients aged ≥18 y	Inpatients and outpatients	COVID-19 *ICD-10* codes (B34.2, B97.29, J12.81, U07.1, U07.2) or laboratory-confirmed COVID-19	Substance use disorder
Egede et al,[21] 2021	Unknown beginning to July 2020	Froedtert/Medical College of Wisconsin Epic medical record database, which includes data from 5 hospitals and 40 health centers and clinics	One-quarter of the population of southeastern Wisconsin	Inpatients and outpatients	Positive reverse transcription-polymerase chain reaction test	Any mental health disorders with or without physical illness including schizophrenia spectrum disorder, mood disorders (including bipolar disorders and depressive disorders), alcohol misuse and drug misuse
Nemani et al,[8] 2021	March 3 to May 31, 2020	NYULH electronic health record system database, which includes data from more than 260 outpatient office sites and 4 acute care hospitals	Individuals from Manhattan, Brooklyn, and Long Island, New York	Inpatients and outpatients	Positive reverse transcription-polymerase chain reaction test	Schizophrenia spectrum disorder mood disorders (including bipolar disorders and depressive disorders); anxiety disorders
Li et al,[20] 2020	February 15 to May 27, 2020	Yale New Haven Health System database, which includes data from a 5-hospital system	Individuals in the northeast of the United States	Inpatients and outpatients	NA	Psychiatric diagnoses (nonspecified)
Wang et al,[27] 2021	Unknown beginning to July 29, 2020	IBM-Watson Health Explorys database, which includes data from a 360-hospital system across 50 states	20% Of the United States population	Inpatients and outpatients	Diagnostic code (specific to the database)	Psychiatric diagnoses; schizophrenia; bipolar disorders; depressive disorders; attention-deficit/hyperactivity disorder; substance use disorder

Abbreviations: *ICD-10*, *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*; NA, not available; NYULH, NYU Langone Health.

disorders). The funnel plot is presented in eFigure 1 in the Supplement and shows no publication bias (Egger test > 0.05). COVID-19 mortality was associated with an increase in patients with mental health disorders compared with patients without mental health disorders (pooled adjusted OR, 1.38 [95% CI, 1.15-1.65]; I^2 = 0%). In the studies including only patients with severe mental health disorders (schizophrenia spectrum disorders and/or bipolar disorders), the pooled adjusted OR was 1.67 (95% CI, 1.02-2.73; I^2 = 27.3%). In the other studies that included patients with all mental health disorders and addictions, the pooled adjusted OR was 1.34 (95% CI, 1.08-1.65; I^2 = 0%). All *P* values were significant ($P < .05$). The *ICD* codes are presented in eTable 2 in the Supplement and adjustment factors are in eTable 3 in the Supplement.

The forest plots of the crude ORs are presented in eFigure 2 in the Supplement and confirm the abovementioned results (pooled crude OR, 1.75 [95% CI, 1.40-2.19]; I^2 = 26.1%). In studies including only patients with severe mental health disorders, the pooled crude OR was 2.26 (95% CI, 1.18-4.31; I^2 = 55.5%; eFigure 3 in the Supplement). In the other studies that included patients with all mental health disorders and addictions, the pooled crude OR was 1.72 (95% CI, 1.45-2.04; I^2 = 0%). All *P* values were significant ($P < .05$).

The subgroup analyses did not report any significant difference in either the crude or adjusted OR. Comparing patients with each mental health disorder in head-to-head comparisons or patients with severe mental health disorders with those with nonsevere mental health disorders was not possible because in all studies including patients with nonsevere mental health disorders except 1,[8] patients with nonsevere mental health disorders were combined with patients severe mental health disorders.[9,19-21,27,30]

The number of studies reporting ICU admission (4 studies) was not sufficient to perform a meta-analysis. Among this small number of studies, the results were very heterogeneous and contradictory between countries, with an OR less than 1 in France[7] for schizophrenia, 1 in South Korea[9] for all mental health disorders (1 unpublished study by G.F. et al), and more than 1 in the US for patients with alcohol and substance misuse.[22]

Discussion

We confirmed that mental health disorders were associated with increased COVID-19–related mortality from population-based data from 7 countries on 3 continents (North America, Europe, and Asia). Thus, patients with mental health disorders should have been targeted as a high-risk population for severe forms of COVID-19, requiring enhanced preventive and

Table 2. Crude and Adjusted Mortality Odds Ratio

Source	Topic	No.	Age, mean (SD)	%		OR (95% CI)			
						Mortality		ICU admission	
				Men	Mortality	Crude	Adjusted	Crude	Adjusted
Denmark									
Reilev et al,[24] 2020	SZ and BD	76	NA	NA	2.3	3.8 (2.1-7.0)	2.5 (1.2-5.1)	NA	NA
	Alcohol misuse	298	NA	NA	6.4	2.7 (1.9-3.9)	1.8 (1.2-2.7)	NA	NA
	Substance use	185	NA	NA	3.6	2.4 (1.5-3.8)	1.8 (1.1-3.2)	NA	NA
France									
Fond et al,[7] 2021	SZ	823	69.2 (14.6)	48.8	25.6	1.25 (1.05-1.49)	1.30 (1.08-1.56)	0.78 (0.65-0.94)	0.75 (0.62-0.91)
Unpublished study by Fond et al	BD	480	70.9 (13.5)	37.9	26.0	1.30 (1.16-1.45)	1.29 (1.15-1.44)	1.08 (0.97-1.20)	1.02 (0.91-1.14)
Israel									
Tzur-Bitan et al,[26] 2021	SZ	649	NA	NA	3.4	NA	NA	NA	NA
South Korea									
Lee et al,[9] 2020	MD	1443	59.5 (17.2)	39.6	6.7	1.39 (1.01-1.95)	1.38 (1.00-1.95)	1.17 (0.82-1.68)	1.18 (0.82-1.70)
	Severe MD[a]	404[a]	58.7 (17.3)[a]	55.9[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]
Lee et al,[11] 2020	MD	255	77.2 (7.5)	42.7	13.7	1.38 (0.86-2.21)	NA	NA	NA
Jeon et al,[10] 2021	MD	928	61.2 (18.2)	40.2	6.03	7.12 (4.87-10.39)	3.93 (2.57-6.03)	NA	NA
	SZ[a]	159[a]	NA[a]	NA[a]	3.8[a]	NA[a]	2.25 (0.36-14.03)[a]	NA[a]	NA[a]
	BD and MDD[a]	273[a]	NA[a]	NA[a]	4.4[a]	NA[a]	2.33 (0.96-5.66)[a]	NA[a]	NA[a]
Spain									
Pobladór-Plou et al,[19] 2020	Men with BD and MDD	70	NA	100	NA	NA	1.38 (0.98-1.95)	NA	NA
	Men with AD	38	NA	100	NA	NA	0.80 (0.53-1.21)	NA	NA
	Women with BD and MDD	132	NA	0	NA	NA	1.46 (1.12-1.91)	NA	NA
	Women with AD	83	NA	0	NA	NA	1.21 (0.90-1.64)	NA	NA
United Kingdom									
Yang et al,[25] 2020	MD	442	NA	NA	27.1	NA	NA	NA	NA
United States									
Allen et al,[22] 2020	Alcohol and substance use disorder	395	NA	NA	NA	1.20 (0.76-1.90)	0.91 (0.53-1.57)	3.20 (2.29-4.48)	2.61 (1.80-3.79)
Baillargeon et al,[23] 2020	Substance use disorder	5450	53.8 (17.3)	52.4	4.7	NA	1.00 (0.84-1.20)	NA	NA
Egede et al,[21] 2021	MD with physical illness	505	54.0 (17.8)	33.5	7.7	1.52 (0.99-2.32)	1.35 (0.85-2.08)	NA	NA
	MD without physical illness	52	37.7 (15.8)	34.6	1.9	0.39 (0.05-2.86)	1.08 (0.15-8.05)	NA	NA
Nemani et al,[8] 2021	SZ	75	59.7 (15.0)	56.0	26.7	2.93 (1.75-4.92)	2.67 (1.48-4.80)	NA	NA
	BD and MDD	564	62.3 (18.7)	39.9	18.4	1.82 (1.45-2.29)	1.14 (0.87-1.49)	NA	NA
	AD	360	54.9 (19.3)	39.7	10.8	0.98 (0.70-1.38)	0.96 (0.65-1.40)	NA	NA
Li et al,[20] 2020	MD	473	NA	NA	44.8	2.3 (1.8-2.9)	1.5 (1.1-1.9)	NA	NA
Wang et al,[27] 2021	MD	3430	NA	NA	8.5	NA	NA	NA	NA
	Alcohol and substance use disorder	1880	NA	NA	9.6	NA	NA	NA	NA

Abbreviations: AD, anxiety disorder; BD, bipolar disorder; ICU, intensive care unit; MD, mental health disorder; MDD, major depressive disorder; NA, not available; OR, odds ratio; SZ, schizophrenia.

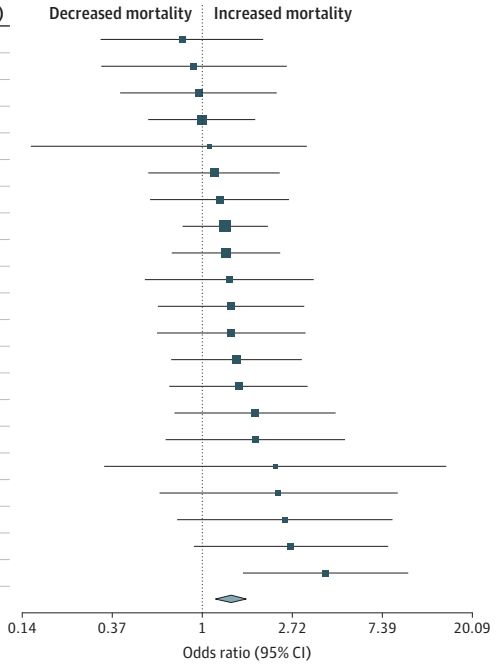
[a] Subgroup analyses.

disease management strategies. However, future studies should evaluate the risk for each mental health disorder, which could not be determined with the current published data.

The different random-effects models confirmed the association between mental health disorders and increased COVID-19-related mortality for both pooled crude and adjusted ORs. The confirmation of increased mortality by adjusted ORs suggests that patients with mental health disorders are at higher risk of poor COVID-19 outcomes than patients without mental health disorders independent of the main clinical risk factors

Figure 2. Forest Plot of the Association Between Mental Health Disorders and Mortality (Adjusted Odds Ratio)

Study	Country	Topic	Odds ratio (95% CI)
Poblador-Plou et al,[19] 2020	Spain	Men with AD	0.80 (0.33-1.97)
Allen et al,[22] 2020	US	AUD and SUD	0.91 (0.32-2.55)
Nemani et al,[8] 2021	US	AD	0.96 (0.40-2.28)
Baillargeon et al,[23] 2020	US	SUD	1.00 (0.55-1.81)
Egede et al,[21] 2021	US	MD without physical illness	1.08 (0.15-7.79)
Nemani et al,[8] 2021	US	BD and MDD	1.14 (0.55-2.36)
Poblador-Plou et al,[19] 2020	Spain	Women with AD	1.21 (0.56-2.61)
Unpublished study by Fond et al	France	BD	1.29 (0.81-2.06)
Fond et al,[7] 2021	France	Schizophrenia	1.30 (0.71-2.37)
Egede et al,[21] 2021	US	MD with physical illness	1.35 (0.53-3.44)
Lee et al,[9] 2020	Korea	MD	1.38 (0.61-3.10)
Poblador-Plou et al,[19] 2020	Spain	Men with BD and MDD	1.38 (0.61-3.14)
Poblador-Plou et al,[19] 2020	Spain	Women with BD and MDD	1.46 (0.71-3.01)
Li et al,[20] 2020	US	MD	1.50 (0.70-3.22)
Reilev et al,[24] 2020	Denmark	AUD	1.80 (0.74-4.39)
Reilev et al,[24] 2020	Denmark	SUD	1.80 (0.67-4.85)
Jeon et al,[10] 2021	Korea	Schizophrenia	2.25 (0.34-14.96)
Jeon et al,[10] 2021	Korea	BD and MDD	2.33 (0.62-8.71)
Reilev et al,[24] 2020	Denmark	Schizophrenia and BD	2.50 (0.76-8.22)
Nemani et al,[8] 2021	US	Schizophrenia	2.67 (0.91-7.81)
Jeon et al,[10] 2021	Korea	MD	3.93 (1.58-9.80)
RE model: $P<.001$; $Q=13.4$; $I^2=0\%$			1.38 (1.15-1.65)



AD indicates anxiety disorder; AUD, alcohol use disorder; BD, bipolar disorder; MD, mental health disorder; MDD, major depressive disorder; SUD, substance use disorder.

for severe COVID-19 (eg, age, obesity, smoking addiction, kidney disease, cardiovascular and cerebrovascular disease, and chronic obstructive pulmonary disease). This suggests that other factors lead to this health inequity in patients with mental health disorders, including several factors such as barriers to access to care, social determinants of health, immunological disturbances, and the effects of psychotropic drugs.

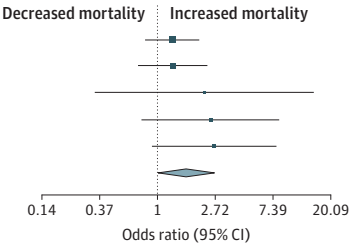
Several studies have reported important barriers to COVID-19–related somatic care in patients with mental health disorders in various countries.[31-36] Therefore, it is likely that these barriers may have influenced access to care during the pandemic and thus had an effect on COVID-19 prognosis in patients with mental health disorders. A wide range of social factors (eg, socioeconomic status, family or household composition, and environmental factors) were also reported to be associated with increased COVID-19 mortality[37] and are known to be highly influential in patients with mental health disorders.[38] These factors need to be explored in depth in future works on mental health disorders and COVID-19, and they need to be considered for health policies.

Patients with schizophrenia and/or bipolar disorders had the highest risk of COVID-19 mortality. This may be explained by the particular immunological profile of these patients. Variation in the human leukocyte antigen complex is one of the most consistently replicated findings in genome-wide association studies in patients with schizophrenia and bipolar disorders.[39] Human leukocyte antigen predominantly regulates viral infection, especially COVID-19.[40] Genetic variability across major human leukocyte antigen class I genes may contribute to differences in the immune response to COVID-19, and an inappropriate T-cell response has been implicated in severe COVID-19 outcomes.[39,41] Abnormal cytokine levels have also been found in the cerebrospinal fluid of patients with schizophrenia and bipolar disorders,[42] who are also at higher risk of hypovitaminosis D,[43,44] contributing to poor COVID-19 prognosis.[45,46] Antipsychotic treatments have shown inconsistent pro- or anti-inflammatory properties, modulating anti-inflammatory (interleukin 4 and interleukin 10) or pro-inflammatory cytokines (interleukin 17, tumor necrosis factor, interferon γ), which results in immune function alterations.[47,48]

In all studies that analyzed patients with depressive disorders, patients with acute major depressive disorder (F32*) and those with recurrent major depressive disorder (F33*) were combined,[8-10] but it is probable that patients with these different forms of the disorder have different risks of COVID-19 mortality. An acute major depressive episode is common, and patients can achieve full remission with or without treatment and without later consequences. In contrast, recurrent major depressive disorder is a severe mental health disorder that may strongly affect functioning and vulnerability to severe COVID-19 events, even between acute episodes. Patients with recurrent major depressive episodes have impaired immune defenses from the onset of illness.[49] However, the administrative databases included in the present work did not include information on the mood state of the patients. It is possible that a current major depressive disorder at COVID-19 onset was the real culprit of increased COVID-19 mortality, and this hypothesis should be further explored. Anxiety disorders have also been associated with immune-inflammatory disturbances[50]; however, the only study that separately ex-

Figure 3. Forest Plot of the Association Between Severe Mental Health Disorders and Mortality (Adjusted Odds Ratio)

Study	Country	Topic	Odds ratio (95% CI)
Unpublished study by Fond et al	France	Bipolar disorder	1.29 (0.81-2.06)
Fond et al,[7] 2021	France	Schizophrenia	1.30 (0.71-2.37)
Jeon et al,[10] 2021	Korea	Schizophrenia	2.25 (0.34-14.96)
Reilev et al,[24] 2020	Denmark	Schizophrenia and bipolar disorder	2.50 (0.76-8.22)
Nemani et al,[8] 2021	US	Schizophrenia	2.67 (0.91-7.81)
RE model: $P = .04$; $Q = 2.6$; $I^2 = 27.3\%$			1.67 (1.02-2.73)



Severe mental health disorders were defined as schizophrenia spectrum disorder and/or bipolar disorder.

plored patients with anxiety disorders did not find an increased risk of COVID-19 mortality in this population.[8]

While addictions are classically distinguished from mental health disorders, patients with addiction were combined with those with mental health disorders in some studies.[10,11,51] Studies analyzing patients misusing alcohol and substances found an increased risk in those patients,[22,23] suggesting that attention should be paid to these patients. Long-term use of tobacco, alcohol, and other drugs is associated with cardiovascular (arrhythmias, cardiac insufficiency, and myocardial infarction), pulmonary (chronic obstructive pulmonary disease, pulmonary hypertension), and metabolic (diabetes, hypertension) diseases,[52,53] all of which are risk factors for COVID-19 infection and worse outcomes. Of note, opioid use disorder is a particular concern in the US. It is estimated that approximately 70 000 people died of an opioid overdose in 2019, and opioids have respiratory depressant effects that could be particularly lethal in the case of COVID-19.[29] As addictions and mental health disorders are frequently comorbid, the contribution of each to mortality risk should be clarified in future studies.

Our study has highlighted that there is a lack of data and discrepant data on ICU admission. Increased ICU admission was found in US patients with COVID-19 with alcohol and/or substance use disorders[22,] while decreased ICU admission was found in French patients with COVID-19 with schizophrenia.[7] ICU admission is an important indicator because it can provide information on the allocation of scarce medical resources. Triage may become necessary when the demand for ICU resources exceeds supply.[54] Severity of illness, initial ward or team the patient was referred from, and do-not-resuscitate order status/patient preference are modifiable factors that could be improved in patient with mental health disorders.[55] Addressing a do-not-resuscitate order is complicated in mental health disorders owing to increased social isolation and the absence of relatives. Advance directives should be implemented in routine mental health to guarantee the respect of patients' wishes, but this remains challenging.[56] Reducing the time of access to the hospital for mental health disorders may prevent them from being admitted with very serious conditions. Specific training on mental health disorders for ICU staff could also deeply reduce mental illness stigma and improve ICU admission of patients with mental health disorders.[57] Future studies should determine the ability of patients with mental health disorders in obtaining health resources in the COVID-19 pandemic.

Strengths and Limitations

The publication bias was reduced at its minimum by the inclusion of population-based approaches of unselected cohorts. Population-based studies allowed complete individual-level ascertainment without restricting analysis to those treated at hospitals and irrespective of socioeconomic differences. Studies yielding no data on patients with positive COVID-19 test results[28] were not included to reduce the heterogeneity of the findings.

Overall, these results should be interpreted with several caveats. Most of the included studies were carried out during the first peak of the COVID-19 pandemic. At this time, testing was largely restricted in some countries (such as the US and France) to symptomatic and high-risk people, while it was provided to all citizens in South Korea, which may explain discrepancies in mortality rates. However, it did not seem to influence the risk of increased mortality in patients with mental health disorders. The important variations in mental health disorder definitions across studies limited our analyses for each mental health disorder and contributed to the heterogeneity of our findings. One study included patients with insomnia and dementia in the mental health disorder group.[11] Insomnia is very common, while dementia is associated with COVID-19 prognosis and should be analyzed separately.[58] One study (published as a letter) did not clearly define its mental health disorder groups.[20]

In light of these issues, we recommend distinguishing data for patients with different mental health disorders in future studies to better understand which patients are at increased risk of COVID-19 mortality. The definition of control groups also varied across studies: some control groups excluded patients with mental health disorders, while others only included patients with or without 1 disorder in a direct head-to-head comparison. We did not obtain information on the stage of illness (acute vs stabilized), which could have affected the risk for severe COVID-19 outcomes. Comorbidities such as obesity or tobacco smoking may often be underreported in medico-administrative databases, thus causing an underestimation of the prevalence of these specific issues. Most of the studies lacked data on social deprivation, which is likely to influence the risk of developing severe COVID-19 or dying.[59] It was not possible to determine if the deaths were directly caused by

COVID-19. No treatment was proven to be effective during the first wave of the COVID-19 pandemic; thus, no treatment data were included in the present analysis because they were available in only 1 study.

Conclusions

In this systematic review and meta-analysis of 16 observational studies involving 19 086 patients with mental health disorders in 7 countries, mental health disorders were associated with increased COVID-19–related mortality after adjustment for the main clinical risk factors for severe COVID-19. Thus, patients with mental health disorders should have been targeted as a high-risk population for severe forms of COVID-19, requiring enhanced preventive and disease management strategies. Future studies should evaluate the risk for each mental health disorder and confirm that patients with schizophrenia and bipolar disorders are at the highest risk of mortality.

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Sent via email (anthony@tjach.org)

September 2, 2021

Anthony Haro, Executive Director
Thomas Jefferson Area Coalition for the Homeless

Dear Anthony,

We are grateful for the addition of Premier Circle to Charlottesville's continuum of services for community members experiencing homelessness. As you know, it is almost impossible for people with mental illness to achieve their recovery goals if they cannot obtain safe and stable housing. Given the COVID pandemic, which is surging again in our community, we understand your priority of utilizing Premier Circle for those most at risk of COVID infection. However, we are concerned that the criteria currently used for determining high risk status excludes some of the most vulnerable members of our community. As a result, we offer the following observations for your consideration:

The CDC list of medical conditions that put people at elevated risk of COVID is by the CDC's own admission not meant to be considered a comprehensive list of such conditions. The list is intended to cite examples of those at high risk only. Relying solely on the list to determine eligibility for Premier Circle means that some high-risk individuals will be denied shelter. These high-risk individuals will disproportionately be people who are elderly, and/or Black or Brown, and/or have disabilities, and/or have a history of incarceration or institutionalization.

In addition to being incomplete, **the CDC list of medical conditions that put people at elevated risk of COVID infection was created to inform patients and medical providers of prudent COVID precautions, *not* determine eligibility for social services**. In part this is because the CDC is aware that "long-standing systemic health and social inequities have put various groups of people at increased risk of getting sick and dying from COVID-19, including many racial and ethnic minority groups.[1]" *In other words, there are experiences apart from medical diagnoses that increase a person's risk for COVID as much, if not more so, than diagnosable medical conditions.*

On July 27[2] and 28[3], 2021, meta-analyses were published in JAMA Psychiatry establishing that people with schizophrenia, bipolar disorder, and major depressive order are at increased risk of morbidity and mortality from COVID infection. While the CDC has not updated its list of

[1] https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

[2] Fond G, Nemani K, Etchecopar-Etchart D, Loundou A, Goff DC, Lee SW, Lancon C, Auquier P, Baumstarck K, Llorca PM, Yon DK, Boyer L. Association Between Mental Health Disorders and Mortality Among Patients With COVID-19 in 7 Countries: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2021 Jul 27:e212274. doi: 10.1001/jamapsychiatry.2021.2274. Epub ahead of print. PMID: 34313711; PMCID: PMC8317055.

[3] Ceban F, Nogo D, Carvalho IP, Lee Y, Nasri F, Xiong J, Lui LMW, Subramaniapillai M, Gill H, Liu RN, Joseph P, Teopiz KM, Cao B, Mansur RB, Lin K, Rosenblat JD, Ho RC, McIntyre RS. Association Between Mood Disorders and Risk of COVID-19 Infection, Hospitalization, and Death: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2021 Jul 28:e211818. doi: 10.1001/jamapsychiatry.2021.1818. Epub ahead of print. PMID: 34319365; PMCID: PMC8319830.

high-risk conditions since May, they do identify meta-analyses such as these as the premise for inclusion on their list.[4]

Some people with substance use disorder (SUD) are protected under the Americans with Disabilities Act and the Fair Housing Act. The research used by the CDC to establish SUD as a high-risk condition defines "substance use disorder" to include people addicted to alcohol as well as people who formerly, but not currently, used illegal substances[5]. As you know, both of these populations are protected by the Americans with Disabilities Act and the Fair Housing Act. Using the CDC list of high-risk conditions as eligibility criteria for housing but then excluding substance use disorder from consideration, even though it is on the CDC list, is legally dubious.

Given the above points, we urge you to revisit the eligibility criteria for Premier Circle. If, during the pandemic, eligibility for housing cannot be determined on the basis of unsheltered status and VI-SPADT score alone, we request you also consider the person's race and ethnicity, disability status, and diagnosis of schizophrenia, bipolar disorder, and major depressive disorder, in addition to using the conditions currently on the CDC list. We also urge you to reconsider your decision to exclude substance use disorder as a qualifying condition for applicants to Premier Circle who are protected by the Americans with Disabilities Act and the Fair Housing Act due to their disease of addiction.

We are grateful for all of the community investment to launch Premier Circle and your ongoing work to manage and administer its services. Premier Circle is a much-needed addition to Charlottesville's continuum of care. Our collective mission includes working with and advocating for community members most vulnerable to discrimination, criminalization, and institutionalization. We hope our efforts are seen in that spirit.

Thank you in advance for your consideration of recommendations. We eagerly await your response.

Sincerely,

Anna Mendez
Executive Director, Partner for Mental Health

Ben Allen, Ed.D
Executive Director, University of Virginia Equity Center

Lisa Dailey, J.D.
Acting Executive Director, Treatment Advocacy Center

Mary T. Giliberti, J.D.
Executive Vice President of Policy, Mental Health America

Neal S. Goodloe, MPA
Criminal Justice Planner, Jefferson Area Community Criminal Justice Board

Kathy Harkey, MAPP, BSP, BSMDS
Executive Director, National Alliance on Mental Illness of Virginia (NAMI Virginia)

[4] https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/underlying-evidence-table.html
[5] https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/underlying-evidence-table.html

Jodi Herndon, MS, LPC, LSATP
Founder and Owner, Herndon's Hope & Healing

Colonel Martin Kumer
Superintendent, Albemarle Charlottesville Regional Jail

Ashley Reynolds Marshall, J.D.
Deputy Charlottesville City Manager for Racial Equity, Diversity, and Inclusion

Victor McKenzie, Jr.
Executive Director, Substance Abuse and Addiction Recovery Alliance of Virginia (SAARA Virginia)

Amy C. Morris, M.S.
Chief of Probation & Parole District # 9, Charlottesville Probation and Parole

Heather S. Orrock
Acting Executive Director, Virginia Organization of Consumers Asserting Leadership (VOCAL)

Erin Tucker, CPRS
Executive Director, On Our Own

cc: Jayson Whitehead
Executive Director, PACEM

March 5, 2021

Via Email

Dr. Rochelle P. Walensky
Acting Director
Centers for Disease Control and Prevention

Dear Dr. Walensky:

We write to urge the CDC to add serious mental illness to the list of health conditions that pose an increased risk to adults of severe illness from the virus that causes COVID-19.

As you know, this list is a critical driver of states' decisions concerning who receives priority for COVID-19 vaccinations as well as strategies to address COVID-19 and decisions concerning allocation of personal protective equipment and other resources. While multiple studies have shown that people with psychiatric disabilities—and particularly people with serious mental illness—have higher rates of hospitalization, morbidity and mortality due to COVID-19 than others, the high risk faced by these individuals has not been widely recognized. We know of only one state, Delaware, that includes serious mental illness among the high-risk conditions that qualify individuals for vaccination priority.

Further, we urge the CDC to highlight strategies to reduce the census in long-term care and correctional facilities as part of its guidance on COVID-19 infection control measures in these facilities. Census reduction is a critical strategy to enable the social distancing that the CDC recommends but measures to secure census reduction are missing from the CDC's guidance.

Recognizing Serious Mental Illness as a High-Risk Health Condition

A substantial number of studies have identified the high risk of contracting COVID-19, hospitalization, and death faced by individuals with psychiatric disabilities.[1] Further, four

[1] *See* Victor Mazereel et al., *COVID-19 vaccination for people with severe mental illness: why, what, and how?*, Lancet, Feb. 3, 2021, https://www.thelancet.com/action/showPdf?pii=S2215-0366%2820%2930564-2 (identifying eight studies); Katlyn Nemani et al., *Association of Psychiatric Disorders With Mortality Among Patients With COVID-19*, J. Amer. Med. Ass'n, at E1, https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2775179.

studies found a "higher risk for worse COVID-19-related outcomes" for people with serious mental illness than for people with less serious mental illness. And most recently, a significant study published in the Journal of the American Medical Association found that individuals with a diagnosis of schizophrenia were 2.7 times as likely to die from COVID-19 as individuals without psychiatric diagnoses, controlling for demographic factors such as age, race and sex and for known medical risk factors.[2] In fact, schizophrenia spectrum diagnoses ranked "second behind age in strength of an association among all demographic and medical risk factors examined in this sample."[3]

While a number of states include group homes, institutions, or other congregate settings for people with psychiatric disabilities in a priority category for vaccination, it appears that only Delaware has prioritized individuals with serious mental illness regardless of setting. Delaware's vaccination phase 1c includes individuals aged 16-64 with high-risk medical conditions including "severe and persistent mental/behavioral health conditions." Given the high risk faced by individuals with serious mental illness, their virtual absence from state vaccination priority lists is striking. It is urgent that the CDC add serious mental illness to its list of high-risk medical conditions, including so that the risks faced by this group of individuals will receive wider recognition.

Including Census Reduction as an Infection Control Strategy in Long-Term Care Facilities

In addition, we urge you to add to the CDC's guidance on infection control in nursing homes and other long-term care facilities a recommendation for measures to reduce the census of such facilities. The existing guidance recommends that facilities "implement aggressive social distancing measures (remaining at least 6 feet apart from others)"[4] but nowhere reference the possibility of accelerating discharges to ensure that social distancing is possible within these facilities.

In light of the difficulties of implementing social distancing in these settings, and the need for single rooms for symptomatic individuals pending COVID-19 testing, it is important to highlight strategies to reduce census through increasing the pace of discharges. For example, the CDC might recommend that states (a) identify individuals in congregate settings who could be discharged to their own homes, to the homes of relatives or friends, or to available mental health or other subsidized housing; (b) offer and provide support to individuals' families and friends to encourage them to open their homes to individuals being discharged from congregate care settings; (c) identify available mental health or other housing options, and (d) as needed provide

[2] *Id.*

[3] *Id.* at E6.

[4] CDC, *Preparing for COVID-19 in Nursing Homes*, updated Nov. 20, 2020, https://www.cdc.gov/coronavirus/2019-ncov/hcp/long-term-care.html.

short-term housing at a hotel or other community setting to allow individuals to isolate/quarantine before moving in with family or friends or into mental health or other subsidized housing.

Including Vaccination and Census Reduction as an Infection Control Strategy in Jails and Prisons

We urge the CDC to encourage states to prioritize jail inmates and prisoners in the same way they prioritize individuals in long-term care facilities to receive the vaccine. About 25% of individuals in jails and 15% of individuals in prisons have a serious mental illness.[5] The overrepresentation of ethnic minorities in such settings, particularly African Americans, is noteworthy and reflective of the social injustice and inequities inherent in our criminal justice system. Given that correctional settings do not readily allow for social distancing, it is not surprising that approximately one in five prisoners have contracted Covid-19[6] and far too many have died as a result. According to the CDC website, there is wide variation in how state vaccination allocation schemes treat state and local correctional facilities.

As with long-term care facilities, consideration should also be given to reducing the census in correctional settings to reduce the spread of Covid-19. Others have outlined important considerations for protecting vulnerable prisoners from COVID-19 that include de-carceration strategies.[7]

Thank you for your prompt attention to these urgent matters. We look forward to working with you and are happy to answer any questions that you may have.

---

[5] Marcus Berzofsky & Jennifer Bronson, Indicators of Mental Health Problems Reported by Prisoners and Jail Inmates, 2011-2012 1, Bureau of Just. Stat. (June 2017), https://www.bjs.gov/content/pub/pdf/imhprpji1112.pdf.

[6] PBS Newshour Weekend, 1 in 5 prisoners in the U.S. has had COVID-19, 1,700 have died (Dec. 19, 2020), https://www.pbs.org/newshour/health/1-in-5-prisoners-in-the-us-has-had-covid-19-1700-have-died.

[7] Akiyama, M.J., Spaulding, A.C., & Rich, J.D. (2020). Flattening the Curve for Incarcerated Populations — Covid-19 in Jails and Prisons. *The New England Journal of Medicine, 382*, 275-277. DOI: 10.1056/NEJMp2005687; Hawks, L., Woolhandler, S., & McCormick, D. COVID-19 in Prisons and Jails in the United States, *JAMA Intern Med, 180*(8):1041-1042. doi:10.1001/jamainternmed.2020.1856; Oladeru, O.T., Tran, N., Al-Rousan, T., Williams, B., & Zaller, N. (2020). A call to protect patients, correctional staff and healthcare professionals in jails and prisons during the COVID-19 pandemic. *Health & Justice, 8*(17).

Sincerely,

American Psychological Association

Judge David L. Bazelon Center for Mental Health Law

Mental Health America

National Alliance on Mental Illness

National Association of State Mental Health Program Directors

Statement on the Need for a National Strategy to Maximize COVID-19 Vaccination for People with Serious Mental Illness

April 2021

The Administration must give urgent, immediate attention to developing and implementing a strategy for vaccinating people with severe mental illness. People with severe mental illness experienced some of the worst mortality disparities pre-pandemic, and are some of the most vulnerable Americans, with a life expectancy up to 25 years lower than the general population. Disparities based on mental illness are often magnified by disparities related to poverty, race or other factors that create barriers to timely health care. New data suggests that many people with severe mental illness will die from preventable COVID-19 infection unless swift action is taken.

Serious mental illness gives rise to an increased risk of infection, hospitalization, and death from COVID-19. Several factors contribute to this increased risk including lack of access to healthcare and housing, obesity linked with medication side effects, and high rates of smoking compared to the population at large.

According to research published in *JAMA Psychiatry* this January, **a schizophrenia diagnosis is the second largest predictor of mortality from COVID-19**, after age. This alarming finding means, and leading scientific experts agree, that we must prioritize people with severe mental illness for COVID-19 vaccination.

But vaccinating this population will not be as simple as making those with severe mental illness eligible to seek an appointment. Beyond the limited availability of the COVID-19 vaccine itself, we must address vaccine hesitancy, limited access to health care and overall lack of resources. All of these factors contribute to make it less likely that people with severe mental illness will receive vaccinations without a clear strategy designed to meet their needs.

Only 25% of adults with severe mental illness receive the annual flu vaccine, compared to almost 50% of adults in the general population. Without a strategically designed vaccination program able to bring the vaccine to people with serious mental illness, they will continue to die potentially preventable deaths in greater numbers than the rest of the public from COVID-19.

As states expand the list of qualifying conditions, we must develop strategies that go beyond eligibility alone, which leaves individuals with severe mental illness to both find and obtain the vaccine from a challenging patchwork of providers and does nothing to address myths causing vaccine hesitancy or avoidance of health and mental health care systems due to past negative experiences. We must employ

strategies that recognize this context and meet people with SMI where they are. We created a national strategy to bring the vaccine directly to senior citizens in acknowledgment of these challenges, and we must do the same for individuals with severe mental illnesses and specifically address those who may experience multiple disparities based on race, ethnicity and severe mental illness.

As leaders of mental health organizations who have seen the devastating effects of COVID 19 on people with severe mental illness, we ask policy makers and health officials to take immediate action to serve those most at risk. Do not sacrifice individuals with severe mental illness to this pandemic or accept their higher mortality rate as inevitable. People with schizophrenia and bipolar disorder deserve better. We call on our state and national leaders to:

- Immediately include people with serious mental illness in the Phase 1C vaccine priority distribution group, as a threshold issue. CDC guidance on this point should be made available to states, pharmacies, and others distributing and administering the vaccine.
- Provide guidance and funding to state and local health departments to establish COVID-19 vaccination programs specifically designed to increase vaccination rates for people with mental illness. These must include mobile vaccine clinics for aggregate housing facilities, robust outreach to at-risk populations at homeless shelters and encampments, engagement by peer support specialists, training of community health workers, nurses and other public health workers, and efforts to address sources of vaccine hesitancy in this population.
- Allocate vaccines to inpatient psychiatric hospitals, community mental health centers, community behavioral health organizations, and other mental health and substance use service providers who are best positioned to reach those with serious mental illness.
- Include peer support specialists in the public health workforce, including community health centers and public health agencies. Peer support specialists should be deployed to specifically address vaccination-related emotional or mental health stressors for individuals with severe mental illness, including providing educational resources about and support in obtaining and attending vaccination appointments.
- Create multi-media materials for states and local communities to provide education about the importance of vaccination and dispelling myths about vaccine safety tailored to those with serious mental illness.
- Gather and publish data on the vaccination rates of people with severe mental illness and whether subgroups of people who experience multiple disparities are getting access to vaccines.

As President Biden said in his address to the nation on the one-year anniversary of the national shutdown due to COVID-19 on March 11, the most important function of the government is to protect the American people. We must start with those most in need of government action and protection from this deadly virus.

American Psychiatric Association
American Psychological Association
(The) Kennedy Forum
Mental Health America
National Alliance on Mental Illness
National Association for Behavioral Healthcare
National Association of Peer Supporters
National Council for Behavioral Health
Treatment Advocacy Center
Well Being Trust

THE HILL

We need a national vaccinatio strategy for people with sever mental illness

BY LISA DAILEY AND PAUL GIONFRIDDO, OPINION CONTRIBUTORS — 04/21/21 03:31 PM EDT
THE VIEWS EXPRESSED BY CONTRIBUTORS ARE THEIR OWN AND NOT THE VIEW OF THE HILL

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COVID-19 and our nation's response to it magnifies a sad truth: We have ignored our fellow citizens with severe mental illness.

When we ignore those citizens, we're leaving behind people with many more barriers to vaccination than the average person. Studies show those living with serious mental illness experience a lack of knowledge and awareness about immunization, a lack of accessibility, a cost barrier, fears about immunization and often no recommendation to receive an immunization from a primary care provider.

Only 25 percent of adults with severe mental illness receive the annual flu vaccine, compared to almost 50 percent of adults in the general population. Without a strategically designed vaccination program able to bring the vaccine to people with serious mental illness, potentially preventable deaths will occur from COVID-19.

According to a bombshell report published in *JAMA Psychiatry* this January, a schizophrenia diagnosis is the second largest predictor of mortality from COVID-19, after age. Based on this alarming finding, leading scientific experts agree we must minimize the barriers to vaccination and maximize access to vaccines for people with severe mental illness.

Just In...

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In fascinating study, researchers show how music spreads just like a virus

As everyone becomes eligible to receive a vaccine, we must develop strategies that go beyond eligibility alone. We created a national strategy to bring the vaccine directly to senior citizens in acknowledgment of the challenges they faced and we must do the same for individuals with severe mental illnesses. We cannot sacrifice individuals with severe mental illness to this pandemic or accept their higher mortality rate as inevitable. People with schizophrenia and bipolar disorder deserve better.

As leaders of mental health organizations who have seen the devastating effects of COVID-19 on people with severe mental illness, we're calling on our state and national leaders to provide guidance and funding to state and local health departments to establish COVID-19 vaccination programs specifically designed to increase vaccination rates for people with mental illness. These must include mobile vaccine clinics for aggregate housing facilities, robust outreach to at-risk populations at homeless shelters and encampments, engagement by peer support specialists, training of community health workers, nurses and other public health workers and efforts to address sources of vaccine hesitancy in this population.

Here's how to put this strategy into action:

First, we must allocate vaccines to inpatient psychiatric hospitals, community mental health centers, community behavioral health organizations and other mental health and substance use service providers who are best positioned to reach those with serious mental illness.

Second, we must create multimedia materials for states and local communities to provide education about the importance of vaccination and dispelling myths about vaccine safety tailored to those with serious mental illness.

Third, we must include peer support specialists in the process — they can connect with those with serious mental illness on a personal level. These peer support specialists should be deployed to community health centers and public health agencies to address emotional or mental health stressors related to vaccination for individuals with severe mental illness.

DeSantis's new surgeon general opposes vaccine mandates

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Fourth, we must gather and publish data on the vaccination rates of people with severe mental illness and determine whether subgroups of people who experience multiple disparities are getting access to vaccines.

As President Biden said in his address to the nation on March 11, the one-year anniversary of the national shutdown due to COVID-19, the most important function of the government is to protect the American people. We must start with those most in need of government action and protection from this deadly virus.

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