RESEARCH LETTER

Association Between Antipsychotic Use and COVID-19 Mortality Among People With Serious Mental Illness

Schizophrenia spectrum disorders are associated with increased mortality in the setting of COVID-19 infection.[1-3] Among several possible explanations for this increased risk is the role of adverse effects of antipsychotic medication, which has not been systematically examined in this population. Our goal was to investigate whether antecedent antipsychotic use was associated with mortality among patients with serious mental illness diagnosed with COVID-19.

Methods | We conducted a retrospective cohort study using the New York University Langone Health electronic health record

Table 1. Characteristics of Study Population by Antipsychotic Use

Characteristic	Antipsychotic use, No. (%) (N = 464)		*P* value[a]
	Yes	No	
No. of patients	196 (42.2)	268 (57.8)	
Age, median (IQR), y	59 (39.5-68.5)	56 (38-66)	.10
Sex			
Female	98 (50.0)	127 (47.4)	.58
Male	98 (50.0)	141 (52.6)	
Race			
Asian	7 (3.6)	6 (2.2)	.54
Black	31 (15.8)	51 (19.0)	
White	116 (59.2)	145 (54.1)	
Other[b]	28 (14.3)	49 (18.3)	
Unknown	14 (7.1)	17 (6.3)	
Ethnicity			
Hispanic[c]	33 (16.8)	45 (16.8)	>.99
Non-Hispanic	163 (83.2)	223 (83.2)	
Smoking status			
Current	28 (14.3)	47 (17.5)	.79
Former	50 (25.5)	64 (23.9)	
Never	106 (54.1)	143 (53.4)	
Missing data	12 (6.1)	14 (5.2)	
Insurance type			
Private	38 (19.4)	78 (29.1)	.05
Public	144 (73.5)	171 (63.8)	
Self-pay	14 (7.1)	19 (7.1)	
Neighborhood poverty level, (below FPL)[d]			
Very high (≥30%)	11 (5.6)	12 (4.5)	.56
High (≥20%)	28 (14.3)	47 (17.5)	
Medium (≥10%)	73 (37.2)	87 (32.5)	
Low (<10%)	83 (42.4)	122 (45.5)	
Psychiatric diagnosis			
Schizophrenia spectrum disorder[e]	91 (46.4)	91 (34.0)	.007
Bipolar disorder	105 (53.6)	177 (66.0)	
BMI, median (IQR)	29.8 (25.8-34.0)	28.2 (24.3-32.4)	.02
Hypertension	118 (60.2)	142 (53)	.12
Myocardial infarction	17 (8.7)	26 (9.7)	.71
Diabetes	72 (36.7)	80 (29.9)	.12
Chronic kidney disease	63 (32.1)	80 (29.9)	.60
Obstructive lung disease	72 (36.7)	97 (36.2)	.91
Inpatient visits, median (IQR), No.	1 (0-2)	1 (0-2)	.12
Ambulatory visits, median (IQR), No.	10 (2-28)	10 (1-29)	.48
Duration, median (IQR), y	3.4 (1.0-4.8)	3.5 (1.2-5.6)	.16
Inpatient	101 (51.5)	118 (44)	.11
Died	21 (10.7)	20 (7.5)	.22

Abbreviations: IQR, interquartile range; FPL, federal poverty level; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FPL, federal poverty level; IQR, interquartile range.

[a] Reported *P* values for χ^2 test or Fisher exact test for categorical variables and *t* test for continuous variables.

[b] Other included Native American, multiple races, and other race by patient report.

[c] Hispanic ethnicity included Chicano/Chicana, Costa Rican, Cuban, Dominican, Guatemalan, Hispanic/Latino, Honduran, Mexican, Mexican American, Nicaraguan, Salvadoran, South American, Spaniard.

[d] Neighborhood poverty level was missing for 1 subject in the antipsychotic treatment group.

[e] Includes diagnoses of schizophrenia and schizoaffective disorder.

Table 2. Multivariable-Adjusted Risk Model for 60-Day Case Fatality

Variable	Odds ratio (95% CI)	*P* value
Antipsychotic use (yes)	1.00 (0.48-2.08)	.99
Insurance type		
Private	1.09 (0.10-12.02)	>.99
Public	1.11 (0.13-9.58)	
Self-pay	1 [Reference]	
Age	1.11 (1.07-1.15)	<.001
Psychiatric diagnosis		
Schizophrenia spectrum disorder[a]	2.88 (1.36-6.11)	.006
Bipolar disorder	1 [Reference]	
BMI	0.99 (0.92-1.05)	.66

Abbreviation: BMI, body mass index.

[a] Includes diagnoses of schizophrenia and schizoaffective disorder.

system. Adults diagnosed with COVID-19 infection between March 3, 2020, and February 17, 2021, who had a preexisting diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder (*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes F20, F25, F30, or F31), were included. Individuals with schizophrenia or schizoaffective disorder were assigned to the schizophrenia spectrum disorder group; those with more than 1 diagnosis were categorized hierarchically, as reported previously.[1,4] The exposure of interest was antipsychotic use at COVID-19 diagnosis. Electronic health records were reviewed to verify the accuracy of prescriptions; patients with antipsychotic discontinuation or nonadherence were assigned to the unexposed group. The primary end point was death within 60 days of COVID-19 diagnosis. The following covariates were considered based on their known or hypothesized association with the outcome and potential to confound the association of interest: sociodemographic characteristics, including patient-reported race (Asian, Black, White, or other race [including Native American, multiple races, and any race not included in a list of more than 40 races], and unknown race) and ethnicity (Hispanic [Chicano/Chicana, Costa Rican, Cuban, Dominican, Guatemalan, Hispanic/Latino, Honduran, Mexican, Mexican American, Nicaraguan, Salvadoran, South American, Spaniard] or non-Hispanic), age, and insurance type; psychiatric diagnosis; medical comorbidities, including body mass index; and smoking status (**Table 1**). The study was approved by the institutional review board of the New York University Grossman School of Medicine, with a waiver of informed consent granted based on the determination that there was no more than minimal risk to participants. The final logistic regression model assessed for an association between antipsychotic exposure and mortality using odds ratios and 95% CIs, adjusting for covariates that differed between groups with 2-tailed testing. Covariates of borderline statistical significance ($P < .10$) were included in the final models because of the limited sample size. Analyses were conducted using SAS statistical software, version 9.4 (SAS Institute Inc).

Results | A total of 464 patients (mean [SD] age, 53 [17.1] years; 239 men [51.5%] and 225 women [48.5%]) were included, of which 196 (42.2%) were treated with antipsychotic medication. Forty-one patients (8.8%) died. The 60-day case fatality rate among patients with a schizophrenia spectrum disorder (n = 182) was 13.7%, and the case fatality rate among patients with bipolar disorder (n = 282) was 5.7%. Age, body mass index, insurance type, and psychiatric diagnosis differed between groups and were included in the fully adjusted model (**Table 2**). Antipsychotic treatment was not significantly associated with mortality (odds ratio, 1.00; 95% CI, 0.48-2.08; $P = .99$). However, a diagnosis of a schizophrenia spectrum disorder was associated with a near 3-fold increased risk of mortality compared with bipolar disorder (odds ratio, 2.88; 95% CI, 1.36-6.11; $P = .01$).

Discussion | In this cohort study of adults with serious mental illness diagnosed with COVID-19 infection in a New York City medical system, antipsychotic treatment was not associated with an increased risk of mortality.

A growing body of evidence has suggested that people with schizophrenia spectrum disorders may have an increased risk of fatal illness after COVID-19 infection, but the mechanism is not clear. An association between antipsychotic medication and increased risk of COVID-19 mortality has been reported in population-based studies,[5,6] but these studies did not take psychiatric diagnosis into account. We did not observe an association between antipsychotic use and mortality in this cohort of adults with serious mental illness. Study limitations include the inability to validate psychiatric diagnoses and capture deaths that were not documented in the electronic health record. The limited sample size precluded analysis of individual antipsychotic medications, which may differ in their associated effects. Further research is needed to understand what underlies increased mortality risk in this population to address worsening health disparities.

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Student Substance Use Policies in US Allopathic Medical Schools: A National Study

In response to the increasing recognition of substance use disorders among physicians and heightened awareness of their negative effects, health care institutions and professional societies have proposed substance use policies focused on offering appropriate treatment and reducing stigmatization. However, little is known about substance use policies governing medical students.

One-third of medical students who responded to a 2012 survey reported alcohol abuse or alcohol dependence (1411 of 4402; 32.4%).[1] Medical students also report using other substances, including amphetamines and opioids, albeit at lower rates.[2] Substance use among medical students is particularly concerning because such behaviors in young adulthood may be risk factors for future substance use[3] and clinician impairment risks patient safety.

In 1992, the Association of American Medical Colleges (AAMC) Group on Student Affairs[4] published guidelines for the development of chemical impairment policies for medical schools. To our knowledge, these are the only published national guidelines steering medical schools' development of substance use policies. We examined US allopathic medical schools' current student handbook policies on substance use and the degree to which these policies adhere to AAMC guidelines.

Methods | From August 2020 to January 2021, we attempted to retrieve student handbooks from all 155 accredited allopathic medical schools in the US by first searching school websites and then emailing or calling (if no active email was available) when handbooks were inaccessible online. We included responses obtained within 3 weeks of the initial contact, and we only reviewed policies found in documents that institutions referred to as a "handbook."

We first operationalized each AAMC guideline (**Table 1**).[4] Three authors (P.Z.M., T.L.W., and W.M.) then independently assessed which criteria were met for each policy (0 indicated not met, and 1 indicated met). Discrepancies were resolved via a majority vote. Policies were considered fully adherent to a guideline if all criteria were met; they were considered partially adherent if only some criteria were met.

Table 1. Criteria Operationalization of AAMC Guidelines for the Development of Chemical Impairment Policies for Medical Schools

AAMC guideline[a]	Criterion operationalization
1. Promote student wellness through professional educational and prevention programs concerning chemical dependency and alcohol use	1a. Mention and existence of an educational plan and didactics concerning chemical dependence and alcohol use at this medical school
	1b. Mention and existence of prevention programs concerning chemical dependence and alcohol use within the medical school curriculum at this medical school
2. Recognize that chemical dependency (including alcoholism) is a treatable disease that affects all of society	2. Explicit statement that chemical dependence is a treatable disease that affects physicians
3. Develop an appropriate program to assist students who are impaired due to chemical abuse and publicize it on a yearly basis to all students	3. Existence of an annually updated, detailed protocol addressing academic and treatment concerns for students seeking treatment for substance use
4. Facilitate the potential for recovery for students who are impaired due to chemical abuse and provide support for students in seeking assistance in handling codependent relationships[b]	4a. Publicized referral to mental health services and/or prevention programs
	4b. Mention of the medical school administration's commitment to allowing students to participate in treatment and medical school education
5. Ensure appropriate levels of confidentiality for individuals seeking information, referral, and treatment	5. Explicit statement of confidentiality throughout the entire treatment process, including pretreatment, referral, and posttreatment
6. Provide an environment in which recovering impaired students are able to continue their medical education without stigma, and where possible, facilitate transition to licensure	6a. Mention of waived disciplinary action for students seeking treatment or actively receiving treatment
	6b. Explicit statement that students' history of substance use will not affect evaluation or assessment by evaluators

Abbreviation: AAMC, Association of American Medical Colleges.

[a] The guidelines are from AAMC.[4]

[b] We defined "support" with regard to institutional support to help the student succeed in educational pursuits and not with regard to mental health support.

The Hofstra University Institutional Review Board exempted this study because the project did not involve interaction with human participants. The study followed the Standards for Quality Improvement Reporting Excellence (SQUIRE) reporting guideline.

Results | Of 155 attempts, we obtained 111 medical student handbooks (72%). Of these handbooks, 101 were accessible online. We contacted 54 schools; 26 schools replied and 10 provided handbooks.

Eighty-four schools met 0 (55 [50%]) or 1 guideline (29 [26%]). Only 1 school (1%) met all 6 guidelines. Guideline 1 was met with the highest frequency, with adherence by 36 schools (32%), followed by guideline 3 (27 [24%]), guideline 5 (21 [19%]), guideline 4 (16 [14%]), guideline 2 (14 [13%]), and guideline 6 (2 [2%]) (**Table 2**).

Rates of partial adherence were higher. Fifty-one schools (46%) partially adhered to guideline 1 for education programs about substance use (criterion 1a). Ninety-two schools (83%) partially adhered to guideline 4 for referrals to mental