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The Effects of SSRIs and Antipsychotics on Long COVID Development in a Large Veteran Population

Jerry Bradley [1,*], Fei Tang [2], Dominique Tosi [1,2], Natasha Resendes [1,2] and Iriana S. Hammel [1,2]

[1] Department of Geriatrics and Palliative Care, University of Miami, Miami, FL 33125, USA; dominique.tosi@va.gov (D.T.); natasha.resendes@va.gov (N.R.); iriana.hammel@med.miami.edu (I.S.H.)
[2] Miami Veterans Administration (VA) Healthcare System Geriatric Research Education and Clinical Center (GRECC), Miami, FL 33125, USA; fei.tang@va.gov
* Correspondence: jerry.bradley@va.gov

Abstract: The development of Long COVID is a complex disease process that may be partially driven by neuroinflammation. Antipsychotics have been shown to exert neuroprotective effects under certain conditions. Our study aimed to determine if veterans treated with antipsychotics and/or selective serotonin reuptake inhibitors (SSRIs) for a psychiatric condition had a reduced risk of developing long-term COVID. We conducted a retrospective cohort study with two cohorts of patients based on the COVID-19 wave in which the patient's initial infection occurred (Cohort 1: alpha/beta waves, and Cohort 2: delta/omicron waves) with stratification by age. A multivariate logistic regression model was used to evaluate the association between the use of antipsychotics and Long COVID diagnosis. In Cohort 1, antipsychotic use was associated with 43% and 34% reductions in the odds of developing Long COVID in patients aged <65 and >65 years, respectively. This association was reduced in the second cohort to 11% in patients aged <65 years and without an association over 65 years of age. SSRIs showed no benefit in either age group or cohort. Our results show that antipsychotic use for the treatment of a mental health condition was associated with a reduction in the risk of developing Long COVID, and the magnitude of this reduction varied between COVID-19 cohorts.

Keywords: long COVID; antipsychotics; SSRIs; PTSD; depression

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1. Introduction

Long COVID or post-acute sequelae of COVID-19 (PASC) is a highly complex disease process with a poorly understood pathophysiological mechanism [1,2]. Some proposed mechanisms include vascular endothelial damage with possible microclot formation [3,4], persistent viral infection [5], chronic inflammation with immune dysregulation [6,7], or a combination of these factors. One area of active investigation is understanding how vascular disruptions in the blood–brain barrier may give rise to persistent systemic inflammation, leading to cognitive symptoms such as brain fog and fatigue [8]. Preliminary results have shown that individuals with persistent depression and other cognitive symptoms after infection with COVID-19 experience elevated neuroinflammatory changes in multiple regions of the brain [9]. Neuroinflammation in this setting has been linked to disruptions in neurotransmission and loss of neurogenesis in the hippocampus [10]. These changes can give rise to persistent neuropsychiatric symptoms [11].

The role of selective serotonin reuptake inhibitors (SSRIs) in mitigating neuroinflammation is an evolving area of research. Studies have shown that SSRIs such as fluvoxamine [12] and fluoxetine [13] can mitigate the effects of proinflammatory states in the brain through several beneficial mechanisms [14]. Both major depressive disorder (MDD) [15] and post-traumatic stress disorder (PTSD) [16] have been linked to neuroinflammation. In the setting of Long COVID, which has been postulated to be driven by neuroinflammatory changes, SSRIs might be beneficial [17,18], further suggesting that serotonin levels are reduced in

patients with Long COVID, leading to diminished tryptophan uptake and hypercoagulability [19]. Despite the proposed pathophysiological mechanisms and the role of SSRIs in mediating it, a meta-analysis examining SSRIs in developing Long COVID demonstrated mixed findings [20]. One study accounting for variations in S1R agonist activity in SSRIs has shown benefits in reducing the risk of Long COVID regardless of activity type [21]. However, several smaller studies have reported no benefits [20]. Several factors may influence these mixed results, such as the specific COVID-19 variant [22], vaccination status [23], changes in clinical practice between waves due to the availability of newer treatment options, and the potential for selection bias or small sample sizes in some studies [20]. These findings raise awareness of the need for larger cohort studies that can account for the variability of responses.

The use of antipsychotics has also been proposed as a potential preventive and treatment option for Long COVID [24]. Much of the work examining the interaction between antipsychotics and neuroinflammation has been conducted in patients diagnosed with schizophrenia and other psychotic conditions. These studies found that antipsychotics help reduce multiple inflammatory markers [25] and decrease the risk of COVID-19 infection in long-term hospitalized patients with serious mental illnesses [26]. Specifically, aripiprazole was found in one study to decrease COVID-19 mortality [27], potentially through modification of these immunological pathways and inflammatory states. In a genomic analysis comparing the peripheral blood of COVID-19 drug-naïve patients versus those treated with aripiprazole, it was shown that aripiprazole was capable of modulating multiple genes that were disrupted or dysfunctional. In this study, it was found that the most significant changes were driven by hyper-inflammation [28].

The use of antipsychotics in the treatment of PTSD has been promising because medications such as quetiapine may enhance neurogenesis and inhibit neurodegeneration caused by stress and trauma [29]. Ziprasidone has also been observed to modulate oxidative stress and mitochondrial dysfunction [30], which are disrupted in the pathophysiology of Long COVID [31]. Antipsychotics have been found to inhibit the inflammatory response in BV-2 microglia, which are activated by lipopolysaccharides (LPS) [32]. This association bridges two aspects of Long COVID, as microbiota changes show an increase in LPS-producing bacterial species [33]. LPS can cause the release of pro-inflammatory cytokines and reactive oxygen species, damaging neurons [34] and leading to prolonged cognitive deficits [35]. Despite studies suggesting the anti-inflammatory role of antipsychotics and SSRIs in the treatment of PTSD and MDD [36,37], their relationship with Long COVID has not been well studied.

At present, the pathophysiology of Long COVID appears to be driven to some degree by neuroinflammation [38,39], which might be mitigated by the use of antipsychotics or SSRIs. We hypothesized that in patients with PTSD or MDD, taking antipsychotics or SSRIs would reduce the risk of developing Long COVID. Furthermore, we expect that there will be differences in the outcomes relative to when the patient first contracted COVID-19. Patients who developed infection during the initial waves might experience a higher risk reduction, because there was little or no access to vaccination, COVID-19-specific medications, and COVID-19 treatment protocols. With these protective factors in subsequent waves, the effect of SSRIs and/or antipsychotics in reducing the risk of Long COVID might be diminished.

2. Materials and Methods

We conducted a retrospective cohort study to evaluate the association between the use of antipsychotics used for the treatment of a psychiatric disease and a new diagnosis of Long COVID. Long COVID was identified by the ICD10 code U09.9 in veterans. Two cohorts of patients were studied. Cohort 1 included patients who tested positive for the first time for SARS-CoV-2 infection between 15 March 2020 and 30 November 2020 (Alpha/Beta waves). Cohort 2 included patients who tested positive between 1 July 2021 and 20 February 2022 (Delta/Omicron waves). We included all veterans who had a positive SARS-CoV-2 test (polymerase chain reaction or antigen test) in VA medical centers or clinics during

these two time periods and had at least one of the following diagnoses: anxiety, depression, or PTSD. We excluded patients who died within 60 days of SARS-CoV-2 infection. We used nationwide data from the VHA medical centers from the VA COVID-19 Shared Data Resource. This study was approved by the Institutional Review Board of the Miami Veterans Affairs Healthcare System and exempted from the requirement for informed consent.

Patients were identified as users of antipsychotics or SSRIs if they were prescribed and were using an antipsychotic within the past two years and within seven days after the positive COVID-19 testing. It was considered that the patient was taking the medication if the prescription was active during this time and was dispensed.

For the delta and omicron periods (Cohort 2), we defined "fully vaccinated" at the time of infection as follows: for BNT162b2 and mRNA-1273 vaccines, at least seven days after receiving of the second dose of vaccine, and for Ad26.COV2.S, at least seven days after receiving the first dose of vaccine. An individual was considered to have received a booster dose seven days after receiving the third dose of BNT162b2 and mRNA-1273 vaccine or the second dose of the Ad26.COV2.S vaccine.

The primary outcome was a Long COVID diagnosis as documented by ICD-10 codes: U.09.9 ("Post COVID-19 condition, unspecified"). In Cohort 1, covariates included age, race, ethnicity, sex, BMI, smoking, national Area Deprivation Index (ADI), kidney disease, COPD, diabetes, hypertension, hyperlipidemia, number of primary care visits in the past 24 months (0–5, 6–11, $\geq$12), and rurality (urban, city town, small town/rural). In Cohort 2, we also included the vaccination status and period (delta period vs. omicron period) in addition to the covariates adjusted for Cohort 1. Continuous variables are presented as mean $\pm$ standard deviation, and median with interquartile range. Categorical variables are presented as frequencies and percentages. When information on race, ethnicity, and smoking status was not available, we reported the data as "Unknown". A multivariate logistic regression model was used to evaluate the association between the use of antipsychotics or SSRIs and the diagnosis of Long COVID, after adjusting for the covariates listed above. The association was also evaluated in patients older than 65 years and in those aged 19 to 64 years. Statistical analysis was performed using R (R Project for Statistical Computing, version 4.0.5).

3. Results

3.1. Cohort 1: Baseline Characteristics

For Cohort 1, we identified 48,298 COVID-19-positive veterans who satisfied our inclusion criteria, with a mean age of 56.6 $\pm$ 16.4 years. A total of 41,508 (85.6%) were males, 30,486 (63.1%) were white, and 5860 (12.1%) were Hispanic (Table 1). Long COVID was diagnosed in 2251 (4.7%) patients (Table 1). Of the total, 3356 (7.4%) patients were prescribed an antipsychotic at least once within two years and were still using it seven days after a positive COVID-19 test. Among patients without Long COVID, 3453 (7.5%) were using an antipsychotic; among the patients with Long COVID, 103 (4.6%) were using an antipsychotic (Table 1). Of the total, 9039 (18.7%) patients were prescribed an SSRI at least once within two years and were still using it seven days after a positive COVID-19 test. Among patients without Long COVID, 8579 (18.6%) were using an SSRI; among patients with Long COVID, 460 (20.4%) were using an SSRI (Table 1).

Table 1. Baseline characteristics of Cohort 1.

	Total ***n*** **= 48,298 (100%)**	**No Long COVID** ***n*** **= 46,047 (95.3%)**	**Long COVID** ***n*** **= 2251 (4.7%)**
Age, mean (years) ± SD (median; IQR)	56.6 ± 16.4 (58; 43–71)	56.7 ± 16.5 (58; 43–71)	56.0 ± 14.4 (57; 44–69)
Age Groups, *n* (%)			
19–64	30,201 (62.5%)	28,702 (62.3%)	1499 (66.6%)
≥65	18,097 (37.5%)	17,345 (37.7%)	752 (33.4%)
Male sex, *n* (%)	41,508 (85.6%)	39,603 (86.0%)	1905 (84.6%)
Race, *n* (%)			
White	30,486 (63.1%)	28,975 (62.9%)	1511 (67.1%)
Black	12,429 (25.7%)	12,018 (26.1%)	411 (18.3%)
Asian	439 (0.9%)	496 (1.1%)	24 (1.1%)
American Indian or Alaska Natives	520 (1.1%)	4274 (0·9%)	266 (1.0%)
Native Hawaiian or Other Pacific Islander	480 (1.0%)	457 (1.0%)	23 (1.0%)
Unknown	3944 (8.2%)	3674 (8.0%)	270 (12.0%)
Ethnicity, *n* (%)			
Hispanic	5860 (12.1%)	5137 (11.2%)	723 (32.1%)
Not Hispanic	41,452 (85.8%)	39,977 (86.8%)	1475 (65.5%)
Unknown	986 (2.0%)	933 (2.0%)	53 (2.4%)
Smoking, *n* (%)			
Current	7383 (15.3%)	7097 (15.4%)	286 (12.7%)
Former Smoker	19,395 (40.2%)	18,523 (40.2%)	872 (38.7%)
Never	19,201 (39.8%)	18,214 (39.6%)	987 (43.8%)
Unknown	2319 (4.8%)	2213 (4.8%)	106 (4.7%)
Comorbidity, *n* (%)			
Kidney Disease	11,325 (23.4%)	10,857 (23.6%)	468 (20.8%)
COPD	8461 (17.5%)	8107 (17.6%)	354 (15.7%)
Diabetes	16164 (33.5%)	15,378 (33.4%)	786 (34.9%)
Hypertension	28,626 (59.3%)	27,291 (59.3%)	1335 (59.3%)
Hyperlipidemia	27,797 (57.6%)	26,403 (57.3%)	1394 (61.9%)
Use antipsychotics	3556 (7.4%)	3453 (7.5%)	103 (4.6%)
Use SSRIs	9039 (18.7%)	8579 (18.6%)	460 (20.4%)

3.2. Cohort 2: Baseline Characteristics

For Cohort 2, we identified 121,357 COVID-19-positive veterans who satisfied our inclusion criteria, with a mean age of 52.9 ± 15.7 years. Overall, 99,127 (81.7%) were males, 79,948 (65.9%) were white, and 13,006 (10.7%) were Hispanic (Table 2). Long COVID was diagnosed in 7953 (6.6%) patients. Of the total, 8198 (6.8%) patients were prescribed antipsychotics at least once within two years and were still using them after seven days of a positive COVID-19 test. Among patients without Long COVID, 7704 (6.8%) were using an antipsychotic; among patients with Long COVID, 494 (6.2%) were using an antipsychotic. Of the total, 21,110 (17.4%) patients were prescribed an SSRI at least once within two years and were still using it after 7 days of a positive COVID-19 test. Among patients without Long COVID, 19,574 (17.3%) were using an SSRI; among patients with Long COVID, 1536 (19.3%) were using an SSRI (Table 2).

Table 2. Baseline characteristics of Cohort 2.

	Total ***n*** **= 121,357 (100%)**	**No Long COVID** ***n*** **= 113,404 (93.4%)**	**Long COVID** ***n*** **= 7953 (6.6%)**
Age, mean (years) ± SD (median; IQR)	52.9 ± 15.7 (52; 39–66)	52.6 ± 15.7 (59; 39–66)	56.2 ± 15.2 (57; 43–69)
19–64	88,373 (72.8%)	83,094 (73.3%)	5279 (66.4%)
≥65	32,984 (27.2%)	30,310 (26.7%)	2674 (33.6%)
Male sex, *n* (%)	99,127 (81.7%)	92,700 (81.7%)	6427 (80.8%)
Race, *n* (%)			
White	79,948 (65.9%)	74,328 (65.5%)	5620 (70.7%)
Black	27,811 (22.9%)	26,444 (23.3%)	1367 (17.2%)
Asian	1504 (1.1%)	5439 (1.1%)	250 (1.0%)
American Indian or Alaska Natives	4540 (1.2%)	1420 (1.3%)	84 (1.1%)
Native Hawaiian or Other Pacific Islander	1248 (1.0%)	1153 (1.0%)	95 (1.0%)
Unknown	9602 (7.9%)	8898 (7.8%)	704 (8.9%)
Ethnicity, *n* (%)			
Hispanic	13,006 (10.7%)	11,539 (10.2%)	1467 (18.4%)
Not Hispanic	101,925 (84.0%)	95,817 (84.5%)	6108 (76.8%)
Unknown	6426 (5.3%)	6048 (5.3%)	378 (4.8%)
Smoking, *n* (%)			
Current	23,012 (19.0%)	21,859 (19.3%)	1153 (14.5%)
Former Smoker	44,635 (36.8%)	41,528 (36.6%)	3107 (39.1%)
Never	48,205 (39.7%)	44,819 (39.5%)	3386 (42.6%)
Unknown	5505 (4.5%)	5198 (4.6%)	307 (3.9%)
Comorbidity, *n* (%)			
Kidney Disease	21,017 (17.3%)	19,242 (17.0%)	1775 (22.3%)
COPD	15,271 (12.6%)	13,932 (12.3%)	1339 (16.8%)
Diabetes	30,562 (29.3%)	28,085 (29.0%)	2477 (34.0%)
Hypertension	60,564 (49.9%)	56,025 (49.4%)	4539 (57.1%)
Hyperlipidemia	63,379 (52.2%)	58,666 (51.7%)	4713 (59.3%)
Use antipsychotics	8198 (6.8%)	7704 (6.8%)	494 (6.2%)
Use SSRIs	21,110 (17.4%)	19,574 (17.3%)	1536 (19.3%)

3.3. Association of Use of Antipsychotic Medication with Long COVID

For Cohort 1, after adjusting for covariates, the use of antipsychotic medication was associated with a 38% decrease in the odds of having a Long COVID diagnosis (Adjusted Odds Ratio (aOR) = 0.62, 95% CI: 0.50–0.76) (Table 3). For patients aged younger than 65, the use of antipsychotic medication was associated with a 43% decrease in the odds of having a Long COVID diagnosis (aOR = 0.57, 95% CI: 0.44–0.74). For patients aged 65 and above, the use of antipsychotic medication was associated with a 34% decrease in the odds of having a Long COVID diagnosis (aOR = 0.66, 95% CI: 0.47–0.90) (Table 3).

Table 3. Adjusted OR for the association between using antipsychotic and Long COVID diagnosis.

	# of Users for All	**aOR for All (95% CI)**	**# of Users for Age ≥ 65**	**aHR for Age ≥ 65 (95% CI)**	**# of Users for Age < 65**	**aHR for Age < 65 (95% CI)**
Cohort 1	3345 (7.3%)	0.62 (0.50–0.76)	1286 (8.1%)	0.66 (0.47–0.90)	2059 (6.9%)	0.57 (0.44–0.74)
Cohort 2	8198 (6.8%)	0.92 (0.83–1.01)	2292 (6.9%)	0.95 (0.80–1.11)	5906 (6.7%)	0.89 (0.79–0.99)

aOR = adjusted odds ratio. aHR = adjusted hazard ratio. # = number.

For Cohort 2, after adjusting for the covariates, the use of antipsychotic medication was not associated with a Long COVID diagnosis (aOR = 0.92, 95% CI: 0.83–1.01). However, for patients younger than 65, the use of antipsychotic medication was associated with an 11% decrease in the odds of having a Long COVID diagnosis (aOR = 0.89, 95% CI: 0.79–0.99). For patients of age 65 and above, the use of antipsychotic medication was not found to be associated with decreased odds of having a Long COVID diagnosis (aOR = 0.95, 95% CI: 0.80–1.11) (Table 3).

3.4. Association of Use of SSRI Medication with Long COVID

For Cohort 1, after adjusting for the covariates, the use of SSRIs was not found to be associated with the odds of having a Long COVID diagnosis (aOR = 1.09, 95% CI: 0.98–1.21). No association between SSRI use and the odds of having a Long COVID diagnosis was found in patients younger or older than 65 years (Table 4).

Table 4. Adjusted OR for the association between using SSRIs and Long COVID diagnosis.

	# of Users for All	aOR for All (95% CI)	# of Users for Age ≥ 65	aHR for Age ≥ 65 (95% CI)	# of Users for Age < 65	aHR for Age < 65 (95% CI)
Cohort 1	8687 (19.0%)	1.09 (0.98–1.21)	3307 (20.7%)	1.06 (0.88–1.26)	5380 (18.0%)	1.11 (0.97–1.27)
Cohort 2	21,110 (17.4%)	1.10 (1.03–1.16)	6477 (19.6%)	1.16 (1.05–1.78)	14,633 (16.6%)	1.06 (0.98–1.14)

aOR = adjusted odds ratio. aHR = adjusted hazard ratio. # = number.

For Cohort 2, after adjusting for the covariates, the use of SSRIs was found to be associated with 10% increase in the odds of having a Long COVID diagnosis (aOR = 1.10, 95% CI: 1.03–1.16). For patients younger than 65, the use of SSRIs was not associated with the odds of having a Long COVID diagnosis (aOR = 1.06, 95% CI: 0.98–1.14). However, for patients of age 65 and above, the use of SSRIs was found to be associated with a 16% increase in the odds of having a Long COVID diagnosis (aOR = 1.16, 95% CI: 1.05–1.78) (Table 4).

3.5. Race and Ethnic Outcomes

We further looked at the racial and ethnic differences in the association between the use of antipsychotics and the odds of Long COVID diagnosis. In Cohort 1, both white (OR = 0.58 CI: 0.45–0.75) and Hispanic (OR = 0.53 CI: 0.34–0.79) patients saw a reduction in Long COVID with the use of antipsychotics. This association remained significant for Hispanic patients in Cohort 2 (OR = 0.66 CI: 0.50–0.85) but not for white patients (OR = 0.91 CI: 0.81–1.02). For Black patients, there was no association between antipsychotic use and the odds of having Long COVID in either cohort (Table 5).

Table 5. The association between the use of antipsychotics and Long COVID diagnosis by race.

	Cohort 1 # on Antipsychotics	Cohort 1 aOR (95% CI)	Cohort 2 # on Antipsychotics	Cohort 2 aOR (95% CI)
Black	941 (7.9%)	0.66 (0.42–1.00)	2147 (7.7%)	1.05 (0.86–1.28)
White	2098 (7.3%)	0.58 (0.45–0.75)	5276 (6.6%)	0.91 (0.81–1.02)
Hispanic	324 (5.7%)	0.53 (0.34–0.79)	773 (5.9%)	0.66 (0.50–0.85)

aOR = adjusted odds ratio. # = number.

4. Discussion

4.1. Antipsychotic Use Reduces Risk of Long COVID

To our knowledge, this study is one of the first to show a link between the use of antipsychotics for treatment of a psychiatric condition and a reduction in the risk of developing Long COVID. The first cohort had the strongest effect, with reductions of 43% and 34% in patients aged <65 years and >65 years, respectively. In the second cohort, this effect was diminished in patients aged <65 years (11%) and was not present in patients aged >65 years. These results are expected with the development of COVID-19 treatments [40], vaccinations [23], and other resources that were not widely available during the initial COVID-19 waves. The use of these resources and new treatment approaches in the second cohort may have confounded the risk of Long COVID independent of the use of antipsychotics. Because our study could not assess which patients received these modalities, aside from vaccination status, we could not determine the specific drivers for this reduction in benefit.

4.2. SSRIs Did Not Affect Risk of Long COVID

Our study found that SSRIs did not impact the risk of Long COVID. Although the results of prior studies have been mixed on this issue [20], larger studies have found some protective benefits of using SSRIs [21]. One reason for this difference may be the prevalence of PTSD and MDD in the veteran population [41]. Individuals within these cohorts may have a high disease burden [41], be refractory to treatment, or have other barriers to care that are not typically observed in the non-veteran population [42,43]. All of these factors may have influenced the response of SSRIs and their potential benefits in cases of Long COVID, as seen in other studies. These findings highlight the need for future research to address these factors.

4.3. Antipsychotics and SSRIs in Long COVID

Another point raised by our study is the comparison between antipsychotics and SSRIs based on their effectiveness in reducing the development of Long COVID. Both of these medications have been proposed to mediate the development of neuroinflammation within the brain [14,17], potentially mitigating some of the pathophysiology believed to cause Long COVID [10,39]. Studies have shown that serotonin levels are diminished in patients with Long COVID [26]; therefore, SSRIs would be expected to be beneficial. The effects of antipsychotics may extend beyond their neuronal anti-inflammatory properties and into other secondary effects. Limited data are available on whether this is impacted by modification of genomic expression [28] or its influence on inflammation [44–46]. More research is required to determine the precise mechanisms by which antipsychotics influence the development of Long COVID.

4.4. Race and Ethnic Differences

Regarding racial differences, Black patients did not show a significant change in odds ratios for Long COVID. These findings are critical, as Black patients have been underrepresented in Long COVID diagnosis and management [47,48], despite having a higher likelihood of developing Long COVID, according to some studies [49]. In contrast, Hispanic patients had the lowest odds ratios. These findings are unexpected, as Hispanic patients had higher mortality compared to non-Hispanic whites [50], and higher risks of developing Long COVID [51]. These findings highlight the need for further studies on how racial and ethnic differences and inequality might impact Long COVID diagnosis and treatment.

4.5. Strengths and Limitations

One of the strengths of this study is that it was a large national cohort with the potential to evaluate multiple aspects of the medical records. Another strength is that patients were only included in the study if they had filled the prescription at some point within the previous two years and were still actively filling the prescription for the medication for at least 7 days after the initial COVID-19 infection. One possible limitation of this study is that we could not verify whether the patient was actually taking the medication, even though it was prescribed and dispensed at the pharmacy. Therefore, if the prescription was active during this time and was dispensed, it was counted as if the patient was taking the medication. Another strength of this study is that we analyzed two cohorts of patients diagnosed during specific waves of COVID-19 before the availability of vaccination, improved medical resources, and availability of COVID-19-specific treatments. A limitation of this approach is that we could not determine which of these treatment modalities the patients may have utilized within the second cohort. Additionally, patients were not separated based on inpatient versus outpatient treatment of their initial COVID-19 infection. Therefore, the magnitude of these effects in relation to antipsychotics and SSRIs cannot be fully determined. Because of the limitations of a retrospective study, we could not determine the presence of reinfection, which may have inadvertently increased the risk of developing Long COVID. Finally, we were unable to identify specific types of

antipsychotics or SSRIs owing to database limitations. Some studies have suggested that second-generation antipsychotics might be more effective than other types of antipsychotics in reducing the overall risk of COVID-19 infection [26]. Future prospective research should consider these factors to better determine the effects and interactions of these components.

5. Conclusions

The use of antipsychotics in veterans with mental health conditions reduced the risk of developing Long COVID during the initial COVID-19 wave and in subsequent waves in patients aged <65 years. The use of SSRIs showed no impact in either cohort. Further research is needed to determine the mechanism by which antipsychotics may affect the development of Long COVID to improve the prevention and treatment of this disabling disease.

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Data Availability Statement: The datasets presented in this article are not readily available because of the Department of Veterans Affairs data policies. Requests to access the datasets should be directed to the Department of Veterans Affairs.

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