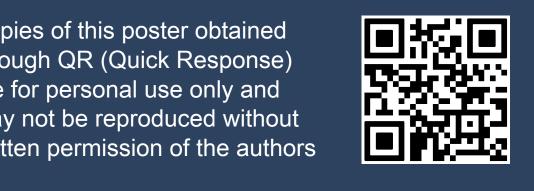
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Conclusions

- Patients aged ≥65 years were prescribed antiviral medications for COVID-19 at higher rates compared with the overall population
- Populations with a high risk for severe COVID-19 (ie, patients aged ≥65 years and patients with immunosuppressive conditions) had higher rates of medication use with potential drug-drug interactions with antiviral therapy
- The majority of these potential drug-drug interactions were with nirmatrelvir/ritonavir¹
- Common approaches for managing these categories of drug-drug interactions, as defined by the National Institutes of Health, involve temporarily withholding or adjusting the concomitant medication dose; these approaches require close monitoring and increased follow-ups, placing substantial burden on both individuals and health care providers
- The prevalence of potential drug-drug interactions in this study highlights the challenges of using currently available oral antivirals, particularly nirmatrelvir/ritonavir, for outpatient treatment of COVID-19 in certain high-risk individuals who face continued risk for severe COVID-19
- Hospitalization rates approximately doubled when patients were not treated for COVID-19, although further evaluation of subgroups is needed to account for potential confounding effects

Plain Language Summary

- Improvements in COVID-19 treatments over time, along with other factors like vaccination, have reduced the chances of having a COVID-19 infection that requires hospitalization
- Drug-drug interactions between antiviral medications used to treat COVID-19 and other common medications pose a safety risk as more people use antiviral therapies in the outpatient setting
- This study used HealthVerity data to analyze outpatient treatment patterns, with a focus on the prevalence of drug-drug interactions
- Older individuals and those with immunosuppressive conditions were given COVID-19 antiviral medications more often and had more drug-drug interactions
- Patients who did not receive antiviral treatment for COVID-19 had twice as many hospitalizations as those who received antiviral treatment; nirmatrelvir/ritonavir was the most common antiviral medication used in this study and had many drug-drug interactions

Introduction

- COVID-19 treatments have rapidly evolved since the beginning of the pandemic, with several medications receiving US Food and Drug Administration emergency use authorization or full approval¹⁻³
- Clinically significant drug-drug interactions (DDIs) have been reported between COVID-19 treatments and other therapeutic drugs, presenting significant safety and efficacy concerns for COVID-19 patients⁴⁻⁷
- This study utilized the HealthVerity database to analyze COVID-19 treatment patterns, patient characteristics, and the prevalence of DDIs in the outpatient setting during the Omicron era

Methods

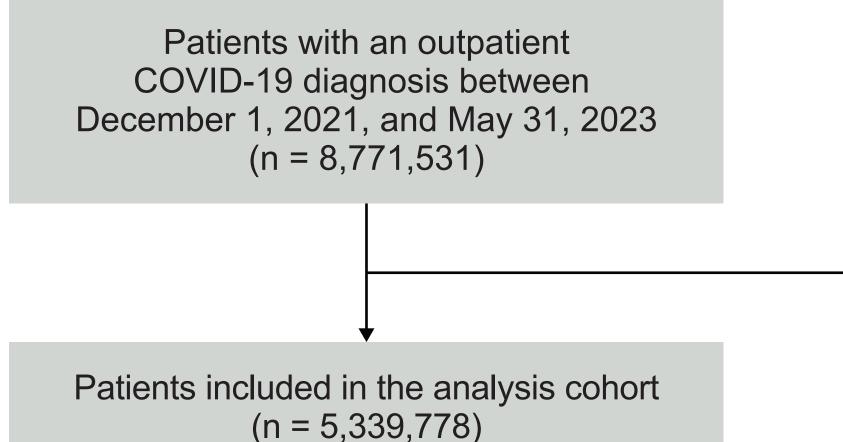
- Data for this retrospective, observational analysis were obtained from HealthVerity Real-Time Insights and Evidence, a unified database of chargemaster, electronic health record, and claims data
- Closed payer claims data were derived from the insurance provider (or payer) and captured nearly all events that occurred
- during a patient's enrollment period, including medical and pharmacy visits and transactions for both retail and specialty settings • The analysis included patients aged ≥12 years with an outpatient COVID-19 diagnosis between December 1, 2021, and May 31, 2023, with ≥180 days of medical history in chargemaster or claims data prior to diagnosis and ≥90 days of follow-up
- post diagnosis • Patients were excluded if they had participated in a clinical trial within 28 days of the index date (outpatient COVID-19 diagnosis date)
- Demographics, Charlson Comorbidity Index score, and medication prescription history were analyzed for all patients and for patients in high-risk subpopulations (ie, patients aged ≥65 years and patients with immunosuppressive conditions, including hematologic malignancies, HIV/AIDS, organ transplant, rheumatologic/inflammatory conditions, solid malignancy, or other immune conditions)8
- Any active medication prescriptions with potential DDIs with COVID-19 antiviral therapy (ie, nirmatrelvir/ritonavir, remdesivir, and molnupiravir) 90 days prior to diagnosis were captured
- Antiviral therapy ≤7 days post diagnosis and any hospitalization ≤30 days post diagnosis were also captured

Results

Participants

• A total of 5,339,778 patients met the inclusion criteria during the study period and were included in the analysis (Figure 1)

Figure 1. Patient Attrition



Did not meet inclusion criteria or met exclusion criteria (n = 3,431,753)

- No medical claims from the index date to ≥90 days after (n = 1,234,668)
- No pharmacy claims from the index date to ≥90 days after (n = 986,967)
- Did not have ≥1 claim ≥180 days prior to the index date (n = 31,760)
- COVID-19 diagnosis during an inpatient hospitalization on the index date (n = 196,894) Clinical trial participation within 28 days of the index date (n = 1261)
- Age <12 years or missing age (n = 980,203)

The index date was the date of outpatient COVID-19 diagnosis. Claims data were derived from the insurance provider (or payer) and captured during a patient's enrollment period, including medical and pharmacy visits and transactions for both retail and

- The population aged ≥65 years was prescribed antiviral medication at higher rates compared with the overall population, whereas patients with immunosuppressive conditions had a similar rate of antiviral prescriptions to that of the overall population (Table 1)
- Receipt of any COVID-19 antiviral medications increased over time, with <1% of patients receiving treatment from January to March 2022

(<1% nirmatrelvir/ritonavir) compared with 26% of patients (24% nirmatrelvir/ritonavir) from October to December 2022

Table 1. Characteristics of Patients Diagnosed With COVID-19 in the Outpatient Setting^a

Characteristic	Overall (n = 5,339,778)	Patients Aged ≥65 Years (n = 600,447)	Patients With Immunosuppressive Conditions (n = 142,731)
Female, n (%)	3,338,663 (63)	349,253 (58)	88,833 (62)
Age, years, median (IQR)	40.0 (26.0-56.0)		57.0 (43.0-68.0)
Age group, n (%)			,
<18 years	598,232 (11)	_	3613 (3)
≥18-<50 years	2,832,768 (53)	_	46,055 (32)
≥50-<65 years	1,308,331 (25)	_	49,587 (35)
≥65 years	600,447 (11)	600,447 (100)	43,476 (30)
Region, n (%)	· · · ·		· · ·
Northeast	1,116,774 (21)	181,542 (30)	37,881 (27)
Midwest	1,129,780 (21)	116,680 (19)	31,497 (22)
South	2,080,965 (39)	165,862 (28)	43,614 (31)
West	995,081 (19)	125,692 (21)	28,864 (20)
Other/missing	17,178 (<1)	10,671 (2)	875 (1)
Charlson Comorbidity Index score, n (%)			
0	3,584,446 (67)	176,486 (29)	31,309 (22)
1	935,654 (18)	120,003 (20)	23,508 (16)
2	368,506 (7)	101,117 (17)	23,615 (17)
≥3	451,172 (8)	202,841 (34)	64,299 (45)
Immunosuppressive condition, n (%)	142,731 (3)	43,476 (7)	_
Hematologic malignancies	6499 (<1)	2392 (<1)	6499 (5)
HIV/AIDS	5988 (<1)	723 (<1)	5988 (4)
Organ transplant	7342 (<1)	1398 (<1)	7342 (5)
Other immune conditions	12,559 (<1)	2493 (<1)	12,559 (9)
Rheumatologic/inflammatory conditions	64,915 (1)	17,848 (3)	64,915 (45)
Solid malignancy	54,999 (1)	22,253 (4)	54,999 (39)
Any COVID-19 antiviral prescription ≤7 days after diagnosis, n (%)	596,398 (11)	113,088 (19)	15,595 (11)
Specific antiviral prescription ≤7 days after diagnosis, ^b n (%)			
Molnupiravir	61,881 (1)	14,902 (2)	1669 (1)
Nirmatrelvir/ritonavir	535,028 (10)	98,308 (16)	13,814 (10)
Remdesivir	958 (<1)	263 (<1)	168 (<1)
Insurance, n (%)			
Commercial	2,457,702 (46)	134,115 (22)	51,709 (36)
Medicaid	2,453,409 (46)	123,738 (21)	62,010 (43)
Medicare Advantage	432,668 (8)	348,534 (58)	29,496 (21)

^aPercentages may not sum to 100% due to rounding. Patients may have had ≥1 prescription during this period and may have been counted more than once

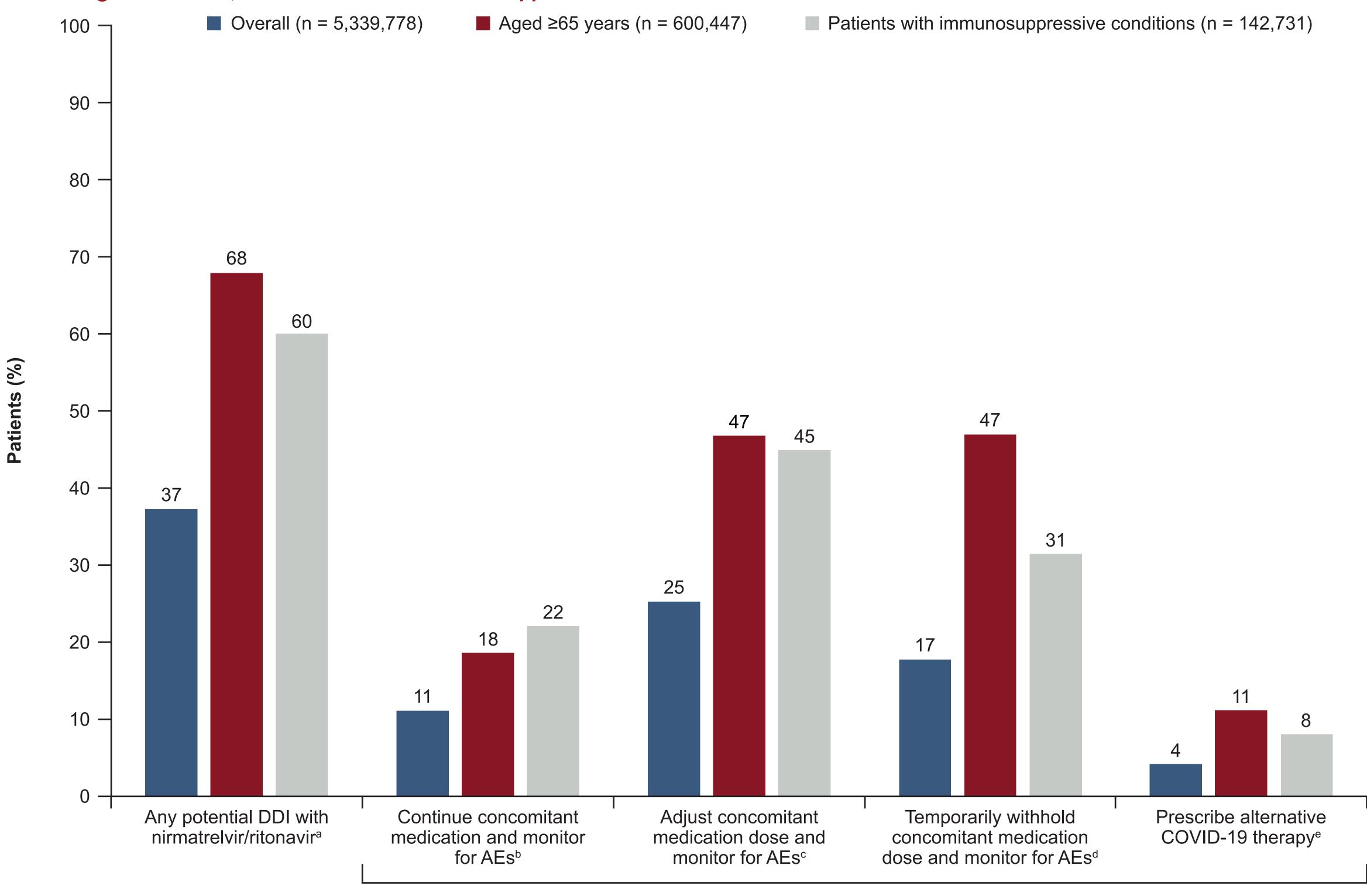
Katherine Townsend, PhD, of Lumanity Communications Inc., and were funded by Gilead Sciences, Inc.

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- Overall, 37% of the total study cohort used medications with potential DDIs with nirmatrelvir/ritonavir 90 days prior to the index date; a small proportion (<1% overall) had potential DDIs with remdesivir (Figure 2)
- As most potential DDIs were with nirmatrelvir/ritonavir, additional analysis of subgroups and DDI types was performed for this antiviral treatment
- The use of medications with potential DDIs was higher in patients aged ≥65 years and in those with immunosuppressive conditions compared with the overall population

— For these high-risk populations, the most common DDI responses were to adjust the concomitant medication dose and monitor for adverse events or to temporarily withhold the concomitant medication

Figure 2. Use of Medications With Potential DDIs With Nirmatrelvir/Ritonavir Within 90 Days of Outpatient Diagnosis for the Overall Population, Patients Aged ≥65 Years, and Patients With Immunosuppressive Conditions



Management Recommendation of Potential DDI With Nirmatrelvir/Ritonavir

^bNIH indicates that pre-emptive dose adjustment is not required but may be considered based on an individualized assessment of the patient's risk for AEs ^cNIH suggests reducing the dose or extending the dosing interval of the concomitant medication.

dNIH indicates that the medications should be withheld during nirmatrelvir/ritonavir treatment and for ≥2 to 3 days after treatment completion

eNIH indicates that management strategies are not possible or feasible, or the risks outweigh the potential benefits. AE, adverse event; DDI, drug-drug interaction; NIH, National Institutes of Health.

Hospitalization Rates

- Overall, 2% of patients had an inpatient hospitalization ≤30 days post COVID-19 diagnosis
- Among patients who were treated for COVID-19, <1% were hospitalized ≤30 days post diagnosis while 2% of patients who were untreated were hospitalized (Table 2)

Table 2. Rates of All-cause Hospitalization ≤30 Days Post Diagnosis for Patients Treated and **Not Treated for COVID-19**

	Overall (n = 5,339,778)	Patients Aged ≥65 Years (n = 600,447)	Patients With Immunosuppressive Conditions (n = 142,731)
Inpatient hospitalization ≤30 days post diagnosis, n (%)	94,065 (2)	29,436 (5)	10,702 (7)
Treateda	n = 596,398	n = 113,088	n = 15,595
Inpatient hospitalization, n (%) ^b	5664 (<1)	2324 (2)	548 (4)
Untreated	n = 4,743,380	n = 487,359	n = 127,136
Inpatient hospitalization, n (%) ^b	88,401 (2)	27,112 (6)	10,154 (8)

^aTreatment: antiviral therapy. ^bPercentages for those with inpatient hospitalization in the treated and untreated subgroups were calculated using the total number of treated and untreated patients.

Disclosures: MB, AL, C-YC, AC, and EM are employees of and may own stock or stock options in Gilead Sciences, Inc. CR is an employee of Family Health Centers of San Diego; and has received honoraria/consultant fees from AbbVie, Gilead Sciences, Inc., Pfizer, and ViiV Healthcare, MJ has no conflicts to report.