Machine Learning Identifies Predictors of Delayed or No Remdesivir Use in Hospitalized COVID-19 Patients

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Conclusions

- A machine learning method was used to show that select patient risk factors for COVID-19 influenced the likelihood of receiving delayed or no remdesivir treatment upon hospitalization for COVID-19 when the Omicron variant was dominant in the United States
  - Patients with chronic kidney disease, type 1 or 2 diabetes mellitus, or limited activities of daily living and those who were assumed/considered to be Black showed significantly greater risk of receiving delayed or no remdesivir treatment
  - Patients who were diagnosed with bipolar disorder or who smoked were more likely to receive timely remdesivir treatment
- These results provide insight into factors that have influenced treatment practices, which can inform future efforts to reduce health care disparities and enhance health equity

Plain Language Summary

- Remdesivir is an antiviral drug that is used to treat people in the hospital with COVID-19
- Receiving antivirals, like remdesivir, early during an infection can help people with COVID-19 recover faster than those who receive antivirals late or those who do not receive antivirals
- In this study, claims data from the United States were used to find out which patient traits were connected to receiving remdesivir early versus late or not at all
- We found that people with chronic kidney disease or diabetes, those who were limited in daily activities, and those who were Black were the most likely to receive remdesivir late or not at all
- We also found that people who were diagnosed with bipolar disorder and people who smoked were more likely to get remdesivir early
- These results highlight disparities in the prescription of remdesivir to people who are in the hospital with COVID-19

Introduction

- COVID-19 remains a public health concern despite the availability of effective interventions[1]
- Clinical studies have shown that remdesivir (RDV) reduces mortality, disease progression, and recovery time in individuals hospitalized with COVID-19[2,3]
- Administration of RDV early during the course of infection, when viral replication is at its highest, is important to achieve the greatest clinical benefit[2,4,5]
- Current Infectious Diseases Society of America guidelines recommend RDV treatment for patients who are hospitalized for COVID-19 and at a high risk of disease progression[6]

Objective

- To identify attributes associated with the likelihood of receiving delayed or no RDV treatment during the Omicron period in patients hospitalized for COVID-19

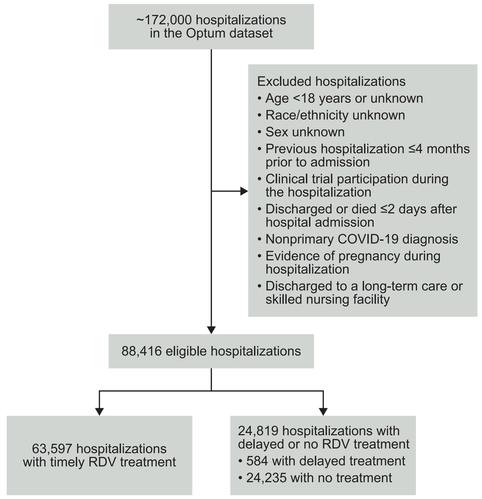
Methods

- This retrospective, observational cohort study was conducted using deidentified patient data from the Optum® Clinformatics® Data Mart database, which included enrollment records, medical claims, pharmacy claims, and laboratory results and was representative of the US population[7]
  - The overall study period (May 2, 2020-December 31, 2023) was broken down into 3 variant periods:
    - Pre-Delta period: May 2, 2020, to May 31, 2021
    - Delta period: June 1, 2021, to November 30, 2021
    - Omicron period: December 1, 2021, to December 31, 2023
  - Data released by Optum in May 2024 were used in this study
- Hospitalizations were included if patients were hospitalized with a primary diagnosis of COVID-19 (identified by the *International Classification of Diseases, Tenth Revision* [ICD-10] code U07.1); aged ≥18 years; continuously enrolled in the database ≥6 months prior to hospitalization, with a permissible gap of ≤31 days; and had known sex, birth year, and race/ethnicity
  - Patients were allowed multiple hospitalizations for COVID-19 within the study period, with a washout period of 4 months between discharge and the subsequent admission; gaps of <2 days between discharge and a subsequent admission were considered a single hospitalization event
- A list of ICD-10 codes for comorbidities associated with a higher risk of COVID-19 diagnosis, grouped into broader risk factor categories, was obtained from the US Centers for Disease Control and Prevention
  - Recursive feature elimination (RFE) was utilized to identify 3456 patient risk factors grouped into 46 categories and demographic characteristics (henceforth referred to as "features") that were associated with receiving delayed (>2 days of hospital admission) or no RDV treatment during each variant period
  - Features identified by RFE for any variant period were included as potential predictors for multivariate logistic regression; the risk of delayed or no RDV treatment for each risk factor category was estimated for each variant period

Results

- In total, 88,416 hospitalizations met the eligibility criteria (**Figure 1**)

Figure 1. Hospitalizations Included in the Study Dataset



RDV, remdesivir.

- Baseline demographic features in the dataset were generally similar across variant periods (**Table 1**)

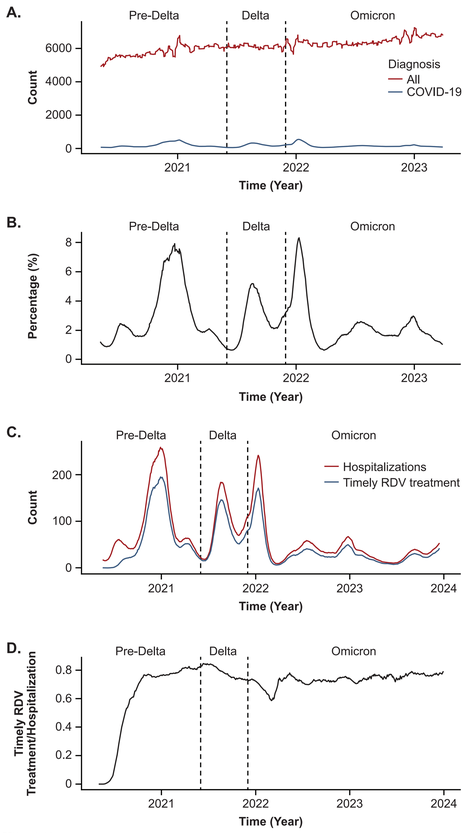
Table 1. Baseline Demographic Features

Feature, n (%)	Variant Period		
	Pre-Delta May 2, 2020-May 31, 2021 (n = 35,915)	Delta Jun 1, 2021-Nov 30, 2021 (n = 17,022)	Omicron Dec 1, 2021-Dec 31, 2023 (n = 35,479)
Sex			
Female	17,456 (49)	8344 (49)	18,242 (51)
Male	18,459 (51)	8678 (51)	17,237 (49)
Race/ethnicity[a]			
White	25,037 (70)	12,969 (76)	27,478 (77)
Black	6033 (17)	2452 (14)	4826 (14)
Asian	1232 (3)	456 (3)	1109 (3)
Hispanic	3613 (10)	1145 (7)	2066 (6)
Age group			
<50 years	1686 (5)	1760 (10)	878 (2)
≥50 years	34,229 (95)	15,262 (90)	34,601 (98)

[a]Only 1 race or 1 ethnicity was associated with each hospitalization. Race/ethnicity data were imputed by a third party if self-reported data were not available.

- Of the 35,479 hospitalizations from the Omicron period, 25,780 (73%) had timely RDV treatment
- The number (%) of daily COVID-19 hospitalizations in the study population peaked at 338 (8%) in the Pre-Delta period, at 227 (5%) in the Delta period, and at 294 (8%) in the Omicron period (**Figure 2A-B**)
  - The number of timely RDV treatments was consistently lower than the number of COVID-19 hospitalizations in each variant period (**Figure 2C**)
  - The ratio of timely RDV treatments to hospitalizations was highest at the beginning of the Delta period and decreased during the Omicron period (**Figure 2D**)

Figure 2. Hospitalization Count by Diagnosis (A), Percentage of COVID-19 Hospitalization (B), COVID-19 Hospitalization and Timely RDV Treatment Counts (C), and Timely RDV Treatment/COVID-19 Hospitalization (D) Over Time



RDV, remdesivir.

- During the Omicron period, patients were more likely to receive delayed or no RDV treatment if they had chronic kidney disease (37% more likely), had type 1 diabetes mellitus (26% more likely), had type 2 diabetes mellitus (10% more likely), had limited activities of daily living (15% more likely), or were Black (14% more likely; **Table 2**)
  - In contrast, patients who were diagnosed with bipolar disorder or who smoked were 23% and 8% more likely, respectively, to receive timely RDV treatment, possibly due to unmeasured confounding

Table 2. Odds Ratio Estimates for Delayed or No RDV Treatment Based on Multivariate Regression During the Omicron Period

Selected Feature[a]	Odds Ratio[b]
Intellectual disabilities	1.39
Chronic kidney disease	1.37***
Type 1 diabetes mellitus	1.26**
HIV	1.23
Limited activities of daily living	1.15***
Disabilities, general	1.14
Race: Black[c]	1.14**
Type 2 diabetes mellitus	1.10**
Other diabetes mellitus	1.06
Cerebral palsy	1.04
Schizophrenia and other psychotic disorders	1.04
Cerebrovascular diseases	1.03
Neurological dementia	1.00
Race: Asian[c]	0.99
Heart disease	0.98
Chronic obstructive pulmonary disease	0.93
Ethnicity: Hispanic[c]	0.93
Limited activities of daily living, reduced mobility	0.92
Smoking	0.92*
Previously hospitalized with COVID-19	0.86
Pulmonary hypertension	0.84
Bipolar disorder	0.77*

*P <0.05; **P <0.01; ***P <0.001.
[a]Included patient risk factor categories and demographic characteristics.
[b]Odds ratios >1 indicate risk of delayed or no treatment. P values were adjusted with Bonferroni correction in each variant period.
[c]For race/ethnicity features, the reference population consisted of White, non-Hispanic patients.
RDV, remdesivir.

Limitations

- The logistic regression model used in this study did not capture potential time-dependent treatment risk factors
- RDV was not approved by the US Food and Drug Administration for use in individuals with severe kidney impairment, including those on dialysis, until July 2023,[8] late into the Omicron period
- Approximately 70% of the race/ethnicity data in the Optum database were imputed by a third party that utilized the patient's name and geography to derive their race/ethnicity, as opposed to self-reporting

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