Supplementary Online Content

Chokkalingam AP, Hayden J, Goldman JD, et al. Association of remdesivir treatment with mortality among hospitalized adults with COVID-19 in the United States. *JAMA Netw Open.* 2022;5(12):e2244505. doi:10.1001/jamanetworkopen.2022.44505

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods.

Data source

HealthVerity Ecosystem, including hospital chargemaster (i.e., transactional data for inpatient and outpatient encounters) and medical and pharmacy claims (open and closed) between December 1, 2018 through May 3, 2021. Linked chargemaster and claims data from this period include approximately 9 million patients from roughly 400 US hospitals nationwide from Veradigm and other nationally represented health plans including both commercial plans as well as Medicaid and Medicare. Laboratory and outpatient electronic health record (EHR) data are available for subsets of individuals.

Study Population

Patients were required to have evidence of activity in the data at least 12 months prior to the index date as well as at least one medical claim or chargemaster record within the 12 months prior to index date. This 12-month lookback window was chosen to permit assessment of baseline comorbidities utilizing linked claims data. Covid-19 diagnosis was defined as International Classification of Disease Revision-10 (ICD-10) diagnosis code U07.1 (Covid-19, virus identified) in any position on a medical claim, inclusive of inpatient hospital encounters. Covid-19 definition made no distinction between nosocomial and community-acquired infections.

Covariates

Comorbid conditions were identified by the presence of at least 1 documented diagnosis or procedure code using a combination of medical and pharmacy claims and chargemaster data in

the year prior to cohort entry. In order to ensure observability of these conditions, we required individuals to have a year of claims or enrollment activity in the year prior to their cohort entry date. Demographic characteristics and Covid-19 severity were assessed on index date, while comorbidities were measured in the 12 months prior to, and excluding, the index date. Concomitant medication use was assessed between hospital admission and index date.

Risk-Set Sampling and Propensity Score-Matching

We identified all patients hospitalized with newly diagnosed Covid-19 between May 1, 2020 and May 3, 2021 and met the eligibility criteria ("eligible patient cohort"). Among this eligible hospitalized patient cohort, a two-stage approach was used to achieve balance in baseline characteristics between remdesivir exposed and matched control patients.

Risk-set sampling. In the first stage, we used 1:1 risk-set sampling (RSS) without replacement ("RSS cohort"). A randomly selected patient who initiated remdesivir ("exposed") was individually matched to a patient randomly selected from Covid-19 patients who were hospitalized ±3 calendar days of the index patient and had not initiated remdesivir ("control"). In addition, control patients had to match on the following criteria:

- age categories of exposed patient (18-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-84, >=85 years)
- sex of exposed patient
- Oxygen support level of exposed patient: room/ambient air (no evidence of oxygen support); low-flow oxygen (supplemental oxygen); high-flow oxygen (e.g., high flow

nasal cannula), or non-invasive ventilation (e.g., CPAP, BIPAP); invasive mechanical ventilation (intubation) or ECMO

- ICU status of exposed patient at admission
- Categorized time (days) since hospital admission of remdesivir-exposure of exposed patient: 0 to 1, 2 to 3, 4 to 5, 6 to 9, 10 to 14, 15 to 19, and ≥ 20 days
- Corticosteroid use of exposed patient

Index date was defined as date of remdesivir initiation for each patient in the remdesivir-exposed cohort and that patient's matched control. Through this RSS sampling, the matched control group included patients who never initiated remdesivir as well as patients who were remdesivir-unexposed at the index date but may have later initiated remdesivir. Creating an RSS cohort allowed us to identify a group of patients that included a control group approximating the standard of care without remdesivir treatment.

Propensity-score matching. In the second stage, we subsequently used the pool of eligible patients in the RSS cohort to perform propensity score matching to identify a subset of remdesivir exposed patients and control patients. We reassigned patient matches to create our final analytic cohort. Propensity score (PS) matching was performed to control for measured confounding, adjusting for potential baseline differences between the treatment and control groups beyond the characteristics accounted for in the RSS-match. Using a logistic regression model, the PS was calculated predicting the probability of remdesivir treatment conditional on

the observed baseline characteristics,[1] including demographics, clinical characteristics, comorbidities, and concomitant medications. Missing data for sex and region were treated as a separate category; there were no missing data for any other variables. The full list of PS covariates and definitions are provided in **eTable 1** (unless otherwise noted in the table). Remdesivir exposed patients were 1:1 matched without replacement to control patients based on the PS, using a 1% caliper. Thus, the control patient with the smallest PS-difference to the exposed patient was selected as the match and became ineligible to be a control for another exposed patient. If a remdesivir exposed patient could not be matched to a control, the patient was excluded from the analysis set. We assessed baseline covariate balance between the exposed and control patients in the RSS cohort as well as the PS-matched cohort using absolute standardized differences, applying a threshold of 0.10 difference to indicate well-balanced groups.[1]

Refer to Figure 1 for the number of patients during each matching stage. eTable 2 shows the baseline characteristics of hospitalized patients meeting the study eligibility criteria and either receiving remdesivir or not receiving remdesivir. eTable 3 presents the baseline characteristics of patients receiving remdesivir included in the final analysis and patients receiving remdesivir but did not match.

Statistical Analysis

For the AT analysis patients were censored on the earliest occurrence of discharge or maximum follow-up of 28 days, and among control patients at the time of crossover to initiation of

[1] Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivariate Behav Res. 2011 May;46(3):399-424. doi: 10.1080/00273171.2011.568786.

remdesivir was also a censoring event. Cause-specific hazards models were applied to the PS-matched cohort to estimate hazard ratios (HR) and 95% confidence intervals (CIs) of remdesivir compared to control patients (α=0.05). No covariates were included in the models as these were well adjusted in the RSS and PS-matching. Subgroup analyses by oxygen requirement status at time of remdesivir initiation were also performed. PS matching was done separately within each oxygen support subgroup.

Lastly, two post-hoc analyses were performed. First, a *post-hoc* competing risk analysis was conducted using the Fine-Gray subdistribution (sd) hazard regression model to estimate hazard ratios (HR_{sd}) and 95% CIs of remdesivir compared to control patients with hospital discharge treated as a competing risk.[2,3,4] Second, a "tipping point" analysis was performed, which calculated the E-value to estimate the minimum strength of an association that an unmeasured confounder would need to have with both the exposure and the outcome to fully explain the observed relationship between remdesivir and inpatient mortality (i.e., shift the HR to the null), conditional on the measured confounders.[5]

[2] Fine J, Gray R. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc*. 1999;(94):496-509.

[3] Austin PC, Fine JP. Accounting for competing risks in randomized controlled trials: a review and recommendations for improvement. *Stat Med*. 2017;36(8):1203-1209. doi:10.1002/sim.7215

[4] Austin PC, Fine JP. Practical recommendations for reporting Fine-Gray model analyses for competing risk data. *Stat Med*. 2017;36(27):4391-4400. doi:10.1002/sim.7501

[5] VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. *Ann Intern Med*. 2017;167(4):268-274. doi:10.7326/M16-2607

eResults.

Patients

Among the 39,775 patients who received remdesivir during an inpatient hospitalization meeting the patient selection criteria, time to remdesivir administration decreased over the 1-year observation period: the mean (SD) time to remdesivir administration changed from 4.6 days (16.87) to 0.4 days (0.82) in the second quarter of 2020 and 2021, respectively (**eFigure 2**).

Before RSS- and PS-matching, hospitalized patients receiving remdesivir and patients not receiving remdesivir differed in important demographics and clinical characteristics, including age, gender, oxygen support and cardiovascular and renal comorbidities (**eTable 2**)**.** There were 9,423 (23.7%) remdesivir-exposed patients who could not be included during the RSS matching phase, followed by 5,496 (18.1%) who could not be PS-matched to a control. Relative to the final remdesivir-exposed cohort, remdesivir-exposed patients who were not RSS-matched tended to be younger and have fewer comorbidities, but had more severe disease, including higher proportions requiring high-flow oxygen/NIV, ECMO/IMV, and ICU support baseline (**eTable 3**).

eTable 1. Definitions for Covariates Included in the PS Model (Unless Otherwise Noted)

Covariate	Definition
Demographic characteristics	
Age	Continuous age
Age Categories *(not included in PS-Match)*	18-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-84, ≥85 years
Sex	Male: 1 - Male (ref) Female: 2 - Female Unknown: (Missing)
Geographic Region	Northeast: 1 - Northeast (ref) (Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont) Midwest: 2 - North Central (Iowa, Illinois, Indiana, Kansas, Michigan, Minnesota, Missouri, North Dakota, Nebraska, Ohio, South Dakota, Wisconsin) South: 3 - South (Alabama, Arkansas, District of Columbia, Delaware, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia) West: 4 - West (Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, New Mexico, Nevada, Oregon, Utah, Washington, Wyoming) Other/Missing/Unknown: 5 - Unknown, (Missing) (Armed Forces Americas, Armed Forces, Armed Forces Pacific, American Samoa, Micronesia, Guam, Marshall Islands, Northern Marianas Islands, Puerto Rico, Palau, Virgin Islands)
Disease severity and hospitalization days	
Oxygen support status	*Room air:* Absence of the below procedures *Low-flow oxygen:* Any of the following procedures occurred: Low-flow oxygen, any oxygen excluding high-flow, non-invasive ventilation (NIV), Invasive Mechanical Ventilation (IMV) or Extracorporeal Membrane Oxygenation (ECMO) *High-flow oxygen/non-invasive ventilation*: Any of the following procedures occurred: Non-invasive ventilation or high-flow oxygen *Invasive mechanical ventilation/ECMO:* Any of the following procedures occurred: ECMO or invasive mechanical ventilation
ICU status	Yes or No
Number of days since hospitalizations	Continuous days

Covariate	Definition
Comorbidities defined by H-CUP CCSR[6]	
Infection	Tuberculosis; Septicemia; Bacterial infections; Fungal infections; HIV infection; Hepatitis; Viral infection; Parasitic, other specified and unspecified infections; Sexually transmitted infections (excluding HIV and hepatitis); Sequela of specified infectious disease conditions
Blood	Nutritional anemia; Hemolytic anemia; Aplastic anemia; Acute posthemorrhagic anemia; Sickle cell trait/anemia; Coagulation and hemorrhagic disorders; Diseases of white blood cells; Immunity disorders; Postprocedural or postoperative complications of the spleen; Other specified and unspecified hematologic conditions
Diabetes	Diabetes mellitus without complication; Diabetes mellitus with complication; Diabetes mellitus, Type 1; Diabetes mellitus, Type 2; Diabetes mellitus, due to underlying condition, drug or chemical induced, or other specified type
Metabolic	Malnutrition; Disorders of lipid metabolism
Obesity	Obesity
Endocrine	Thyroid disorders; Fluid and electrolyte disorders; Cystic fibrosis; Pituitary disorders; Other specified and unspecified endocrine disorders
Digestive	Intestinal infection; Esophageal disorders; Gastroduodenal ulcer; Gastrointestinal and biliary perforation; Gastritis and duodenitis; Other specified and unspecified disorders of stomach and duodenum; Appendicitis and other appendiceal conditions; Regional enteritis and ulcerative colitis; Intestinal obstruction and ileus; Diverticulosis and diverticulitis; Anal and rectal conditions; Peritonitis and intra-abdominal abscess; Biliary tract disease; Hepatic failure; Other specified and unspecified liver disease; Pancreatic disorders (excluding diabetes); Gastrointestinal hemorrhage; Noninfectious gastroenteritis; Noninfectious hepatitis; Postprocedural or postoperative digestive system complication
Neurologic	Meningitis; Encephalitis; Other specified CNS infection and poliomyelitis; Parkinson's disease; Multiple sclerosis; Other specified hereditary and degenerative nervous system conditions; Cerebral palsy; Paralysis (other than cerebral palsy); Epilepsy; convulsions; Neurocognitive disorders; Transient cerebral ischemia; Coma; stupor; and brain damage; CNS abscess; Polyneuropathies; Myopathies; Postprocedural or postoperative nervous system complication
Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified	Chronic phlebitis; thrombophlebitis and thromboembolism; Varicose veins of lower extremity; Post-thrombotic syndrome and venous insufficiency/hypertension; Other specified diseases of veins and lymphatics
Diseases of arteries, arterioles and capillaries	Peripheral and visceral vascular disease; Arterial dissections; Aortic; peripheral; and visceral artery aneurysms; Aortic and peripheral arterial embolism or thrombosis

[6] ICD-10 codes are available from the Agency for Healthcare Research and Quality (AHRQ). Healthcare Cost and Utilization Project (H-CUP). Tools Archived for Clinical Classifications Software Refined. Available from: https://www.hcup-us.ahrq.gov/toolssoftware/ccsr/ccsr_archive.jsp.

Covariate	Definition
Diseases of pulmonary circulation	Acute pulmonary embolism; Pulmonary heart disease
Ischemic heart diseases	Coronary atherosclerosis and other heart disease; Complications of acute myocardial infarction; Acute myocardial infarction
Cerebrovascular disease	Cerebral infarction; Acute hemorrhagic cerebrovascular disease; Sequelae of hemorrhagic cerebrovascular disease; Occlusion or stenosis of precerebral or cerebral arteries without infarction; Other and ill-defined cerebrovascular disease; Sequelae of cerebral infarction and other cerebrovascular disease
Abnormal blood pressure (hyper)	Essential hypertension; Hypertension with complications and secondary hypertension
Abnormal blood pressure (hypo)	Hypotension
Other and unspecified disorders of the circulatory system	Other specified and unspecified circulatory disease; Acute phlebitis; thrombophlebitis and thromboembolism Vasculitis; Postprocedural or postoperative circulatory system complication
Other forms of heart disease	Nonrheumatic and unspecified valve disorders; Myocarditis and cardiomyopathy; Pericarditis and pericardial disease; Other and ill-defined heart disease
Heart failure	Heart failure
Conductive disorders, dysrhythmias	Conduction disorders; Cardiac dysrhythmias; Cardiac arrest and ventricular fibrillation
Rheumatic fever/diseases	Chronic rheumatic heart disease; Acute rheumatic heart disease; Endocarditis and endocardial disease
Renal (Acute)	Nephritis, nephrosis, renal sclerosis; Acute and unspecified renal failure
Renal (Chronic)	Chronic kidney disease
Transplant	Complication of transplanted organs or tissue; Organ transplant status
Genitourinary	Urinary tract infections; Calculus of urinary tract; Other specified and unspecified diseases of kidney and ureters; Other specified and unspecified diseases of bladder and urethra; Hematuria; Proteinuria; Vesicoureteral reflux; Hyperplasia of prostate; Inflammatory conditions of male genital organs; Inflammatory diseases of female pelvic organs
Respiratory	Sinusitis; Pneumonia (except that caused by tuberculosis); Influenza; Acute and chronic tonsillitis Acute bronchitis; Other specified upper respiratory infections; Other specified and unspecified upper respiratory disease; Chronic obstructive pulmonary disease and bronchiectasis; Asthma; Aspiration pneumonitis; Pleurisy, pleural effusion and pulmonary collapse; Respiratory failure; insufficiency; arrest; Lung disease due to external agents; Pneumothorax; Mediastinal disorders; Other specified and unspecified lower respiratory disease; Postprocedural or postoperative respiratory system complication

Covariate	Definition
Mood/Neuro	Schizophrenia spectrum and other psychotic disorders; Depressive disorders; Bipolar and related disorders; Other specified and unspecified mood disorders; Anxiety and fear-related disorders; Obsessive-compulsive and related disorders; Trauma- and stressor-related disorders; Disruptive, impulse-control and conduct disorders; Personality disorders; Feeding and eating disorders; Somatic disorders; Suicidal ideation/attempt/intentional self-harm; Miscellaneous mental and behavioral disorders/conditions; Neurodevelopmental disorders
Behavioral	Alcohol-related disorders; Opioid-related disorders; Cannabis-related disorders; Sedative-related disorders; Stimulant-related disorders; Hallucinogen-related disorders; Inhalant-related disorders; Other specified substance-related disorders; Suicide attempt/intentional self-harm; subsequent encounter; Opioid-related disorders; subsequent encounter; Stimulant-related disorders; subsequent encounter; Cannabis-related disorders; subsequent encounter; Hallucinogen-related disorders; subsequent encounter; Sedative-related disorders; subsequent encounter; Inhalant-related disorders; subsequent encounter; Mental and substance use disorders; sequela
Smoking	Tobacco-related disorders; History of smoking/tobacco use
Musculoskeletal/Connective Tissue	Infective arthritis; Osteomyelitis; Rheumatoid arthritis and related disease; Juvenile arthritis; Other specified chronic arthropathy; Immune-mediated/reactive arthropathies; Spondylopathies/spondyloarthropathy (including infective); Systemic lupus erythematosus and connective tissue disorders; Musculoskeletal abscess; Aseptic necrosis and osteonecrosis; Osteomalacia; Autoinflammatory syndromes
Malformations	Cardiac and circulatory congenital anomalies; Digestive congenital anomalies; Genitourinary congenital anomalies; Nervous system congenital anomalies; Congenital malformations of eye, ear, face, neck; Cleft lip or palate; Respiratory congenital malformations; Musculoskeletal congenital conditions; Chromosomal abnormalities; Other specified and unspecified congenital anomalies
Factors Influencing Health Status	Socioeconomic/psychosocial factors; Lifestyle/life management factors

Covariate	Definition
Neoplasms	Head and neck cancers – eye; Head and neck cancers - lip and oral cavity; Head and neck cancers – throat; Head and neck cancers - salivary gland; Head and neck cancers – nasopharyngeal; Head and neck cancers – hypopharyngeal; Head and neck cancers – pharyngeal; Head and neck cancers – laryngeal; Head and neck cancers – tonsils; Head and neck cancers - all other types; Cardiac cancers; Gastrointestinal cancers – esophagus; Gastrointestinal cancers – stomach; Gastrointestinal cancers - small intestine; Gastrointestinal cancers – colorectal; Gastrointestinal cancers – anus; Gastrointestinal cancers – liver; Gastrointestinal cancers - bile duct; Gastrointestinal cancers – gallbladder; Gastrointestinal cancers – peritoneum; Gastrointestinal cancers - all other types; Respiratory cancers; Bone cancer; Sarcoma; Skin cancers – melanoma; Skin cancers - all other types; Breast cancer - ductal carcinoma in situ (DCIS); Breast cancer - all other types; Female reproductive system cancers – uterus; Female reproductive system cancers – cervix; Female reproductive system cancers – ovary; Female reproductive system cancers - fallopian tube; Female reproductive system cancers – endometrium; Female reproductive system cancers – vulva; Female reproductive system cancers – vagina; Female reproductive system cancers - all other types; Male reproductive system cancers – prostate; Male reproductive system cancers – testis; Male reproductive system cancers – penis; Male reproductive system cancers - all other types; Urinary system cancers – bladder; Urinary system cancers - ureter and renal pelvis; Urinary system cancers – kidney; Urinary system cancers – urethra; Urinary system cancers - all other types; Nervous system cancers – brain; Nervous system cancers - all other types; Endocrine system cancers – thyroid; Endocrine system cancers – pancreas; Endocrine system cancers – thymus; Endocrine system cancers – adrenocortical; Endocrine system cancers – parathyroid; Endocrine system cancers - pituitary gland; Endocrine system cancers - all other types; Hodgkin lymphoma; Non-Hodgkin lymphoma; Leukemia - acute lymphoblastic leukemia (ALL); Leukemia - acute myeloid leukemia (AML); Leukemia - chronic lymphocytic leukemia (CLL); Leukemia - chronic myeloid leukemia (CML); Leukemia - hairy cell; Leukemia - all other types; Multiple myeloma; Malignant neuroendocrine tumors; Mesothelioma; Myelodysplastic syndrome (MDS); Cancer of other sites; Secondary malignancies; Malignant neoplasm, unspecified; Neoplasms of unspecified nature or uncertain behavior; Benign neoplasms; Conditions due to neoplasm or the treatment of neoplasm
Other Signs/Symptoms	Syncope; Shock; Genitourinary signs and symptoms; Circulatory signs and symptoms
Concomitant Medications	
Corticosteroids[7]	"Corticosteroids" used as text string for Hospital Chargemaster Data

[7] Definition of corticosteroids based on following: Barnado A, Casey C, Carroll RJ, Wheless L, Denny JC, Crofford LJ. Developing Electronic Health Record Algorithms That Accurately Identify Patients With Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken). 2017 May;69(5):687-693. doi: 10.1002/acr.22989.

Covariate	Definition
HIV Protease Inhibitors[8]	Pharmacy claims using generic names COBICISTAT", "EMTRICITABINE", "SAQUINAVIR", "TIPRANAVIR", "RITONAVIR" and brand names "REYATAZ", "EVOTAZ", "PREZCOBIX", "TECHNIVIE", "SYMTUZA", "APTIVUS", "RITONAVIR", "INVIRASE", "NORVIR", "KALETRA", "PREZISTA", "VIRACEPT", "CRIXIVAN", "LEXIVA" Additionally, Hospital Chargemaster data using the brand and generic names were searched.
Hydroxychloroquine/Chloroquine[9]	Medical or Pharmacy claims with generic "CHLOROQUINE HCL", "CHLOROQUINE PHOSPHATE", "HYDROXYCHLOROQUINE SULFATE" Or Medical or Pharmacy claims with brand "ARALEN HCL", "ARALEN PHOSPHATE", "QUINEPROX", "PLAQUENIL" Or Medical or Pharmacy claims with procedure J0390 or Hospital Chargemaster data text string "Hydroxychloroquine" was used
Immunomodulators[5]	Included Hospital Chargemaster Data or branded or generic medical or pharmacy claims for Interferon, Tocilizumab, Siltuximab, Sarilumab, Baricitinib, Ribavirin,
Convalescent Plasma[5,10]	Medical claims with procedures P9017, P9071, XW14325, P9099, XW13325 as well as Hospital Chargemaster Data

[8] Definition of HIV Protease Inhibitors from: Paul DW, Neely NB, Clement M, et al. Development and validation of an electronic medical record (EMR)-based computed phenotype of HIV-1 infection. *J Am Med Inform Assoc*. 2018;25(2):150-157. doi:10.1093/jamia/ocx061.

[9] Definition was Aetion derived.

[10] Definition of convalescent plasma also from: Optum360 Coding for Coronavirus (COVID-19). Available from: https://www.optum360coding.com/upload/docs/Optum360%20Coding%20for%20Coronavirus%20Final8.pdf.

eTable 2. Demographic and Clinical Characteristics of Patients Hospitalized for COVID-19 by Administration of Remdesivir Among Hospitalized Patients Meeting the Study Eligibility Criteria (Before Risk Set Sampling)

	Patients not receiving remdesivir N (%)	**Patients receiving remdesivir N (%)**	**Absolute Standardized Difference[a]**
N	73,804	39,775	
Age			
Mean (SD)	63.8 (18.9)	66.4 (15.6)	0.150
Median (IQR)	65 [52, 77]	67 [57, 77]	
Gender			0.115
Female	38,638 (52.4%)	18,532 (46.6%)	
Male	33,600 (45.5%)	20,320 (51.1%)	
Unknown	1,566 (2.1%)	923 (2.3%)	
Region			0.104
Northeast	12,591 (17.1%)	7,232 (18.2%)	
Midwest	6,952 (9.4%)	3,234 (8.1%)	
South	36,830 (49.9%)	18,437 (46.4%)	
West	17,416 (23.6%)	10,858 (27.3%)	
Other/Missing/Unknown	15 (0.0%)	14 (0.0%)	
Baseline Covariates based on CCSR[b]			
Infection	26,980 (36.6%)	11,234 (28.2%)	0.178
Blood	27,287 (37.0%)	10,583 (26.6%)	0.224
Diabetes mellitus	31,087 (42.1%)	15,629 (39.3%)	0.058
Metabolic	52,030 (70.5%)	27,520 (69.2%)	0.029
Obesity	19,659 (26.6%)	10,727 (27.0%)	0.008
Endocrine	18,184 (24.6%)	8,842 (22.2%)	0.057
Digestive	32,612 (44.2%)	15,190 (38.2%)	0.122
Neurologic	40,365 (54.7%)	18,808 (47.3%)	0.149
Diseases of veins, lymphatic vessels and lymph nodes, nec	6,492 (8.8%)	2,763 (6.9%)	0.069
Diseases of arteries, arterioles and capillaries	12,351 (16.7%)	5,382 (13.5%)	0.089
Diseases of pulmonary circulation	5,077 (6.9%)	2,009 (5.1%)	0.077
Ischemic heart diseases	19,247 (26.1%)	9,015 (22.7%)	0.080
Cerebrovascular disease	9,628 (13.0%)	3,831 (9.6%)	0.108
Abnormal blood pressure (hyper)	48,705 (66.0%)	25,059 (63.0%)	0.063

Abnormal blood pressure (hypo)	6,337 (8.6%)	1,912 (4.8%)	0.152
Other and unspecified disorders of the circulatory system	21,728 (29.4%)	9,097 (22.9%)	0.150
Other forms of heart disease	27,306 (37.0%)	11,825 (29.7%)	0.155
Heart Failure	15,593 (21.1%)	6,019 (15.1%)	0.156
Conductive disorders, dysrhythmias	17,401 (23.6%)	7,529 (18.9%)	0.114
Circulatory - Rheumatic fever/diseases	3,265 (4.4%)	1,226 (3.1%)	0.071
Renal (Acute	14,469 (19.6%)	4,793 (12.1%)	0.208
Renal (Chronic)	19,701 (26.7%)	7,273 (18.3%)	0.202
Transplant	1,422 (1.9%)	696 (1.7%)	0.013
Genitourinary	35,185 (47.7%)	15,678 (39.4%)	0.167
Respiratory	39,385 (53.4%)	19,970 (50.2%)	0.063
Mood/Neuro	25,075 (34.0%)	10,390 (26.1%)	0.172
Behavioral	13,112 (17.8%)	4,390 (11.0%)	0.193
Smoking	21,002 (28.5%)	9,208 (23.2%)	0.121
Musculoskeletal/ Connective Tissue	43,725 (59.2%)	22,038 (55.4%)	0.078
Malformations	1,751 (2.4%)	754 (1.9%)	0.033
Factors Influencing Health Status	6,020 (8.2%)	1,808 (4.5%)	0.148
Neoplasms	14,683 (19.9%)	8,090 (20.3%)	0.011
Other Signs/Symptoms	61,453 (83.3%)	31,249 (78.6%)	0.120
Oxygen Support Status[c,d]			0.292
No supplemental oxygen	55,108 (74.7%)	24,500 (61.6%)	
Supplemental oxygen	11,383 (15.4%)	8,590 (21.6%)	
Nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	5,385 (7.3%)	5,308 (13.3%)	
ECMO or IMV	1,928 (2.6%)	1,377 (3.5%)	
ICU	24,839 (33.7%)	14,807 (37.2%)	0.075
# Days since hospitalization			
Mean (SD)	8.8 (9.9)	11.3 (10.4)	0.255
Median (IQR)	6 [4, 10]	8 [6, 13]	
Concomitant medications[d]			
Corticosteroids[e]	37,436 (50.7%)	34,483 (86.7%)	0.842
HIV Protease Inhibitors[f]	147 (0.2%)	46 (0.1%)	0.021
Hydroxychloroquine/Chloroquine	746 (1.0%)	280 (0.7%)	0.033
Immunomodulators[g]	1,346 (1.8%)	2,473 (6.2%)	0.225
Convalescent plasma[h]	1,427 (1.9%)	2,887 (7.3%)	0.256
Other Immunologic Agents	2,950 (4.0%)	1,724 (4.3%)	0.017

Abbreviations: CCSR (Clinical Classifications Software Refined); ECMO (extracorporeal membrane oxygenation); ICU (Intensive Care Unit); IMV (Invasive Mechanical Ventilation); NEC (Not Elsewhere Classified)

a Absolute standardized difference based on Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424.

b Measured 365 days prior to inpatient admission

c Measured in RSS on day of remdesivir administration

d Measured in PS-Match between inpatient admission and remdesivir administration

e "Corticosteroids" used as text string for Hospital Chargemaster Data

f Pharmacy claims using generic names COBICISTAT", "EMTRICITABINE", "SAQUINAVIR", "TIPRANAVIR", "RITONAVIR" and brand names "REYATAZ", "EVOTAZ", "PREZCOBIX", "TECHNIVIE", "SYMTUZA", "APTIVUS", "RITONAVIR", "INVIRASE", "NORVIR", "KALETRA", "PREZISTA", "VIRACEPT", "CRIXIVAN", "LEXIVA"

g Immunomodulators include interferon, tocilizumab, siltuximab, sarilumab; baricitinib, and ribavirin.

h Convalescent plasm defined as medical claims with procedures P9017, P9071, XW14325, P9099, XW13325 as well as Hospital Chargemaster Data

eTable 3. Patient Characteristics of Patients Receiving Remdesivir but Not Included in the Risk Set Sampling-Matched or Propensity Score-Matched Cohorts

Characteristic	Final remdesivir-exposed patients in analysis vs. remdesivir patients who did not RSS-match to either the exposed or control populations			Final remdesivir-exposed patients in analysis vs. remdesivir patients with no PS-match		
	PS-matched patients receiving remdesivir N (%)	Hospitalized patients receiving remdesivir not RSS-Matched[a] N (%)	Absolute Standardized Difference	PS-matched patients receiving remdesivir N (%)	RSS-matched patients receiving remdesivir not PS-matched N (%)	Absolute Standardized Difference[b]
N	**24,856**	**2,328**		**24,856**	**5,496**	
Demographic Characteristics						
Age						
Mean (sd)	66.8 (15.4)	59.0 (20.3)	0.433	66.8 (15.4)	66.7 (14.9)	0.011
Median [IQR]	68 [57, 77]	59 [44., 76.]		68 [57, 77]	67 [57, 76]	
Gender						
Female	11,917 (47.9%)	915 (39.3)	0.592	11,917 (47.9%)	2527 (46.0)	0.043
Male	12,596 (50.7%)	988 (42.4)		12,596 (50.7%)	2901 (52.8)	
Unknown	343 (1.4%)	425 (18.3)		343 (1.4%)	68 (1.2)	
Region						
Northeast	4,062 (16.3%)	358 (15.4)	0.080	4,062 (16.3%)	1603 (29.2)	0.684
Midwest	2,332 (9.4%)	232 (10.0)		2,332 (9.4%)	38 (0.7)	
South	12,235 (49.2%)	1218 (52.3)		12,235 (49.2%)	1557 (28.3)	
West	6,221 (25.0%)	520 (22.3)		6,221 (25.0%)	2293 (41.7)	
Other/Missing/Unknown	6 (0.0%)	0 (0.0)		6 (0.0%)	5 (0.1)	
Baseline Covariates[c]						
Infection	12,630 (50.8%)	734 (31.5)	0.400	12,630 (50.8%)	2863 (52.1)	0.026
Blood	9,823 (39.5%)	632 (27.1)	0.265	9,823 (39.5%)	1299 (23.6)	0.347
Diabetes mellitus	11,081 (44.6%)	862 (37.0)	0.154	11,081 (44.6%)	2123 (38.6)	0.121

Metabolic	19,208 (77.3%)	1534 (65.9)	0.254	19,208 (77.3%)	4061 (73.9)	0.079
Obesity	8,197 (33.0%)	705 (30.3)	0.058	8,197 (33.0%)	1848 (33.6)	0.014
Endocrine	6,687 (26.9%)	490 (21.0)	0.137	6,687 (26.9%)	1197 (21.8)	0.120
Digestive	11,657 (46.9%)	861 (37.0)	0.202	11,657 (46.9%)	2060 (37.5)	0.192
Neurologic	13,991 (56.3%)	1125 (48.3)	0.160	13,991 (56.3%)	2361 (43.0)	0.269
Diseases of veins, lymphatic vessels and lymph nodes, nec	1,937 (7.8%)	171 (7.3)	0.017	1,937 (7.8%)	262 (4.8)	0.125
Diseases of arteries, arterioles and capillaries	3,833 (15.4%)	276 (11.9)	0.104	3,833 (15.4%)	483 (8.8)	0.204
Diseases of pulmonary circulation	1,894 (7.6%)	126 (5.4)	0.090	1,894 (7.6%)	262 (4.8)	0.119
Ischemic heart diseases	7,236 (29.1%)	471 (20.2)	0.207	7,236 (29.1%)	1029 (18.7)	0.245
Cerebrovascular disease	2,938 (11.8%)	202 (8.7)	0.104	2,938 (11.8%)	302 (5.5)	0.226
Abnormal blood pressure (hyper)	17,921 (72.1%)	1326 (57.0)	0.321	17,921 (72.1%)	3483 (63.4)	0.187
Abnormal blood pressure (hypo)	2,088 (8.4%)	112 (4.8)	0.145	2,088 (8.4%)	139 (2.5)	0.260
Other and unspecified disorders of the circulatory system	6,841 (27.5%)	569 (24.4)	0.070	6,841 (27.5%)	932 (17.0)	0.256
Other forms of heart disease	9,804 (39.4%)	674 (29.0)	0.223	9,804 (39.4%)	1278 (23.3)	0.354
Heart Failure	5,158 (20.8%)	368 (15.8)	0.128	5,158 (20.8%)	421 (7.7)	0.382
Conductive disorders, dysrhythmias	6,686 (26.9%)	413 (17.7)	0.221	6,686 (26.9%)	941 (17.1)	0.238
Rheumatic fever/diseases	1,019 (4.1%)	63 (2.7)	0.077	1,019 (4.1%)	90 (1.6)	0.148
Renal (Acute)	6,172 (24.8%)	296 (12.7)	0.314	6,172 (24.8%)	652 (11.9)	0.340
Renal (Chronic)	6,208 (25.0%)	404 (17.4)	0.187	6,208 (25.0%)	306 (5.6)	0.560
Transplant	492 (2.0%)	44 (1.9)	0.006	492 (2.0%)	34 (0.6)	0.120
Genitourinary	11,663 (46.9%)	874 (37.5)	0.191	11,663 (46.9%)	1990 (36.2)	0.219
Respiratory	17,155 (69.0%)	1250 (53.7)	0.319	17,155 (69.0%)	4048 (73.7)	0.103
Mood/Neuro	8,123 (32.7%)	640 (27.5)	0.113	8,123 (32.7%)	1262 (23.0)	0.218
Behavioral	3,470 (14.0%)	318 (13.7)	0.009	3,470 (14.0%)	323 (5.9)	0.273

Smoking	7,639 (30.7%)	545 (23.4)	0.165	7,639 (30.7%)	1261 (22.9)	0.176
Musculoskeletal/Connective Tissue	14,804 (59.6%)	1210 (52.0)	0.153	14,804 (59.6%)	2886 (52.5)	0.142
Malformations	521 (2.1%)	72 (3.1)	0.063	521 (2.1%)	69 (1.3)	0.066
Factors Influencing Health Status	1,416 (5.7%)	132 (5.7)	0.001	1,416 (5.7%)	144 (2.6)	0.155
Neoplasms	5,392 (21.7%)	392 (16.8)	0.123	5,392 (21.7%)	1018 (18.5)	0.079
Other Signs/Symptoms	21,449 (86.3%)	1845 (79.3)	0.187	21,449 (86.3%)	4519 (82.2)	0.112
Oxygen Support Status[d,e]						
No supplemental oxygen	15,947 (64.2%)	1092 (46.9)	0.423	15,947 (64.2%)	3498 (63.6)	0.065
Supplemental oxygen	5,434 (21.9%)	556 (23.9)		5,434 (21.9%)	1116 (20.3)	
Nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	2,706 (10.9%)	461 (19.8)		2,706 (10.9%)	699 (12.7)	
ECMO or IMV	769 (3.1%)	219 (9.4)		769 (3.1%)	183 (3.3)	
ICU	7,361 (29.6%)	1328 (57.0)	0.576	7,361 (29.6%)	1509 (27.5)	0.048
# Days since hospitalization						
Mean (sd)	1.9 (2.5)	14.3 (13.5)	1.287	1.9 (2.5)	1.6 (1.5)	0.133
Median [IQR]	1 [1, 2]	10 [6, 18]		1 [1, 2]	1 [1, 2]	
Concomitant medications[e]						
Corticosteroids[f]	17,507 (70.4%)	2052 (88.1)	0.448	17,507 (70.4%)	4012 (73.0)	0.057
HIV Protease Inhibitors[g]	20 (0.1%)	0 (0.0)	0.040	20 (0.1%)	3 (0.1)	0.010
Hydroxychloroquine/Chloroquine	118 (0.5%)	17 (0.7)	0.033	118 (0.5%)	12 (0.2)	0.044
Immunomodulators[h]	208 (0.8%)	260 (11.2)	0.446	208 (0.8%)	520 (9.5)	0.398
Convalescent plasma[i]	311 (1.3%)	233 (10.0)	0.387	311 (1.3%)	478 (8.7)	0.348
Other Immunologic Agents	1,144 (4.6%)	101 (4.3)	0.013	1,144 (4.6%)	158 (2.9)	0.091

Abbreviations: CCSR = Clinical Classifications Software Refined; ECMO = Extracorporeal membrane oxygenation; ICU = Intensive Care Unit; IMV = Invasive Mechanical Ventilation; NEC = Not Elsewhere Classified; PS = Propensity score; RSS = Risk-set sampling

a patient subsequently started on remdesivir, but at a later hospital day, could serve as a risk-set sampling (RSS)-match for an earlier-treated remdesivir patient. In the initial treatment (IT) analysis, that match would be maintained

whereas in the as-treated (AT) analysis, that match would be censored upon initiation of the control patient to remdesivir active-treatment.

b Absolute standardized difference based on Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424.

c Measured 365 days prior to inpatient admission

d Measured in RSS on day of remdesivir administration

e Measured in PS-Match between inpatient admission and remdesivir administration

f "Corticosteroids" used as text string for Hospital Chargemaster Data

g Pharmacy claims using generic names COBICISTAT", "EMTRICITABINE", "SAQUINAVIR", "TIPRANAVIR", "RITONAVIR" and brand names "REYATAZ", "EVOTAZ", "PREZCOBIX", "TECHNIVIE", "SYMTUZA", "APTIVUS", "RITONAVIR", "INVIRASE", "NORVIR", "KALETRA", "PREZISTA", "VIRACEPT", "CRIXIVAN", "LEXIVA"

h Immunomodulators include interferon, tocilizumab, siltuximab, sarilumab; baricitinib, and ribavirin.

i Convalescent plasm defined as medical claims with procedures P9017, P9071, XW14325, P9099, XW13325 as well as Hospital Chargemaster Data

eTable 4. Patient Characteristics Matched on RSS Status and Matched Further on Propensity Score

Characteristic	RSS patients			Propensity score-matched patients		
	RSS Remdesivir (n=30,352) N (%)	RSS Referent (n=30,352) N (%)	Absolute Standardized Difference	Matched remdesivir (n=24,856) N (%)	Matched Referent (n=24,856) N (%)	Absolute Standardized Difference[a]
Demographic Characteristics						
Age			0.001			0.005
Mean (sd)	66.8 (15.3)	66.8 (15.4)		66.8 (15.4)	66.8 (15.4)	
Median [IQR]	67 [57, 77]	67 [57, 77]		68 [57, 77]	67 [57, 77	
Gender			0.000			0.005
Female	14,444 (47.6%)	14,444 (47.6%)		11,917 (47.9%)	11,906 (47.9%)	
Male	15,497 (51.1%)	15,497 (51.1%)		12,596 (50.7%)	12,621 (50.8%)	
Unknown	411 (1.4%)	411 (1.4%)		343 (1.4%)	329 (1.3%)	
Region			0.223			0.004
Northeast	5,665 (18.7%)	4,440 (14.6%)		4,062 (16.3%)	4,095 (16.5%)	
Midwest	2,370 (7.8%)	3,776 (12.4%)		2,332 (9.4%)	2,341 (9.4%)	
South	13,792 (45.4%)	15,328 (50.5%)		12,235 (49.2%)	12,189 (49.0%)	
West	8,514 (28.1%)	6,802 (22.4%)		6,221 (25.0%)	6,225 (25.0%)	
Other/Missing/Unknown	11 (0.0%)	6 (0.0%)		6 (0.0%)	6 (0.0%)	
Baseline Covariates based on CCSR[b]						
Infection	15,493 (51.0%)	15,997 (52.7%)	0.033	12,630 (50.8%)	12,613 (50.7%)	0.001
Blood	11,122 (36.6%)	13,623 (44.9%)	0.168	9,823 (39.5%)	9,775 (39.3%)	0.004
Diabetes mellitus	13,204 (43.5%)	14,229 (46.9%)	0.068	11,081 (44.6%)	11,057 (44.5%)	0.002
Metabolic	23,269 (76.7%)	23,993 (79.0%)	0.057	19,208 (77.3%)	19,189 (77.2%)	0.002
Obesity	10,045 (33.1%)	10,125 (33.4%)	0.006	8,197 (33.0%)	8,185 (32.9%)	0.001
Endocrine	7,884 (26.0%)	8,793 (29.0%)	0.067	6,687 (26.9%)	6,655 (26.8%)	0.003
Digestive	13,717 (45.2%)	15,281 (50.3%)	0.103	11,657 (46.9%)	11,675 (47.0%)	0.001
Neurologic	16,352 (53.9%)	18,285 (60.2%)	0.129	13,991 (56.3%)	14,013 (56.4%)	0.002

Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified	2,199 (7.2%)	2,781 (9.2%)	0.070	1,937 (7.8%)	1,936 (7.8%)	0.000
Diseases of arteries, arterioles and capillaries	4,316 (14.2%)	5,363 (17.7%)	0.094	3,833 (15.4%)	3,816 (15.4%)	0.002
Diseases of pulmonary circulation	2,156 (7.1%)	2,784 (9.2%)	0.076	1,894 (7.6%)	1,897 (7.6%)	0.000
Ischemic heart diseases	8,265 (27.2%)	9,881 (32.6%)	0.116	7,236 (29.1%)	7,197 (29.0%)	0.003
Cerebrovascular disease	3,240 (10.7%)	4,306 (14.2%)	0.107	2,938 (11.8%)	2,968 (11.9%)	0.004
Abnormal blood pressure (hyper)	21,404 (70.5%)	22,728 (74.9%)	0.098	17,921 (72.1%)	17,902 (72.0%)	0.002
Abnormal blood pressure (hypo)	2,227 (7.3%)	3,479 (11.5%)	0.142	2,088 (8.4%)	2,055 (8.3%)	0.005
Other and unspecified disorders of the circulatory system	7,773 (25.6%)	9,538 (31.4%)	0.129	6,841 (27.5%)	6,805 (27.4%)	0.003
Other forms of heart disease	11,082 (36.5%)	13,506 (44.5%)	0.163	9,804 (39.4%)	9,733 (39.2%)	0.006
Heart Failure	5,579 (18.4%)	7,753 (25.5%)	0.174	5,158 (20.8%)	5,095 (20.5%)	0.006
Conductive disorders, dysrhythmias	7,627 (25.1%)	9,113 (30.0%)	0.110	6,686 (26.9%)	6,647 (26.7%)	0.004
Rheumatic fever/diseases	1,109 (3.7%)	1,620 (5.3%)	0.081	1,019 (4.1%)	1,013 (4.1%)	0.001
Renal (Acute)	6,824 (22.5%)	9,123 (30.1%)	0.173	6,172 (24.8%)	6,157 (24.8%)	0.001
Renal (Chronic)	6,514 (21.5%)	9,706 (32.0%)	0.239	6,208 (25.0%)	6,151 (24.7%)	0.005
Transplant	526 (1.7%)	732 (2.4%)	0.048	492 (2.0%)	482 (1.9%)	0.003
Genitourinary	13,653 (45.0%)	15,350 (50.6%)	0.112	11,663 (46.9%)	11,645 (46.8%)	0.001
Respiratory	21,203 (69.9%)	21,189 (69.8%)	0.001	17,155 (69.0%)	17,163 (69.0%)	0.001
Mood/Neuro	9,385 (30.9%)	10,781 (35.5%)	0.098	8,123 (32.7%)	8,172 (32.9%)	0.004
Behavioral	3,793 (12.5%)	5,145 (17.0%)	0.126	3,470 (14.0%)	3,499 (14.1%)	0.003
Smoking	8,900 (29.3%)	10,181 (33.5%)	0.091	7,639 (30.7%)	7,641 (30.7%)	0.000
Musculoskeletal/ Connective Tissue	17,690 (58.3%)	18,699 (61.6%)	0.068	14,804 (59.6%)	14,741 (59.3%)	0.005
Malformations	590 (1.9%)	735 (2.4%)	0.033	521 (2.1%)	531 (2.1%)	0.003
Factors Influencing Health Status	1,560 (5.1%)	2,076 (6.8%)	0.072	1,416 (5.7%)	1,421 (5.7%)	0.001
Neoplasms	6,410 (21.1%)	6,816 (22.5%)	0.032	5,392 (21.7%)	5,410 (21.8%)	0.002

Other Signs/Symptoms	25,968 (85.6%)	26,682 (87.9%)	0.069	21,449 (86.3%)	21,451 (86.3%)	0.000
Oxygen Support Status[c,d]			0.000			0.004
No supplemental oxygen	19,445 (64.1%)	19,445 (64.1%)		15,947 (64.2%)	15,967 (64.2%)	
Supplemental oxygen	6,550 (21.6%)	6,550 (21.6%)		5,434 (21.9%)	5,402 (21.7%)	
Nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both	3,405 (11.2%)	3,405 (11.2%)		2,706 (10.9%)	2,721 (10.9%)	
ECMO or IMV	952 (3.1%)	952 (3.1%)		769 (3.1%)	766 (3.1%)	
ICU	8,870 (29.2%)	9,255 (30.5%)	0.028	7,361 (29.6%)	7,374 (29.7%)	0.001
# Days since hospitalization			0.095			0.022
Mean (sd)	1.8 (2.3)	2.1 (3.1)		1.9 (2.5)	1.9 (2.3)	
Median [IQR]	1. [1, 2]	1 [1, 2]		1 [1, 2]	1 [1, 2]	
Concomitant medications[d]						
Corticosteroids[e]	21,519 (70.9%)	20,916 (68.9%)	0.043	17,507 (70.4%)	17,459 (70.2%)	0.004
HIV Protease Inhibitors[f]	23 (0.1%)	34 (0.1%)	0.012	20 (0.1%)	22 (0.1%)	0.003
Hydroxychloroquine/Chloroquine;	130 (0.4%)	156 (0.5%)	0.013	118 (0.5%)	119 (0.5%)	0.001
Immunomodulators[g]	728 (2.4%)	218 (0.7%)	0.136	208 (0.8%)	218 (0.9%)	0.004
Convalescent plasma[h]	789 (2.6%)	318 (1.0%)	0.116	311 (1.3%)	317 (1.3%)	0.002
Other Immunologic Agents	1,302 (4.3%)	1,547 (5.1%)	0.038	1,144 (4.6%)	1,143 (4.6%)	0.000

Abbreviations: CCSR = Clinical Classifications Software Refined; ECMO = Extracorporeal membrane oxygenation; ICU = Intensive Care Unit; IMV = Invasive Mechanical Ventilation; NEC = Not Elsewhere Classified; PS = Propensity score; RSS = risk-set sampling

a Absolute standardized difference based on Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424.

b Measured 365 days prior to inpatient admission

c Measured in RSS on day of remdesivir administration

d Measured in PS-Match between inpatient admission and remdesivir administration

e “Corticosteroids” used as text string for Hospital Chargemaster Data

f Pharmacy claims using generic names COBICISTAT”, “EMTRICITABINE”, “SAQUINAVIR”, “TIPRANAVIR”, “RITONAVIR” and brand names “REYATAZ”, “EVOTAZ”, “PREZCOBIX”, “TECHNIVIE”, “SYMTUZA”, “APTIVUS”, “RITONAVIR”, “INVIRASE”, “NORVIR”, “KALETRA”, “PREZISTA”, “VIRACEPT”, “CRIXIVAN”, “LEXIVA”

g Immunomodulators include interferon, tocilizumab, siltuximab, sarilumab; baricitinib, and ribavirin.

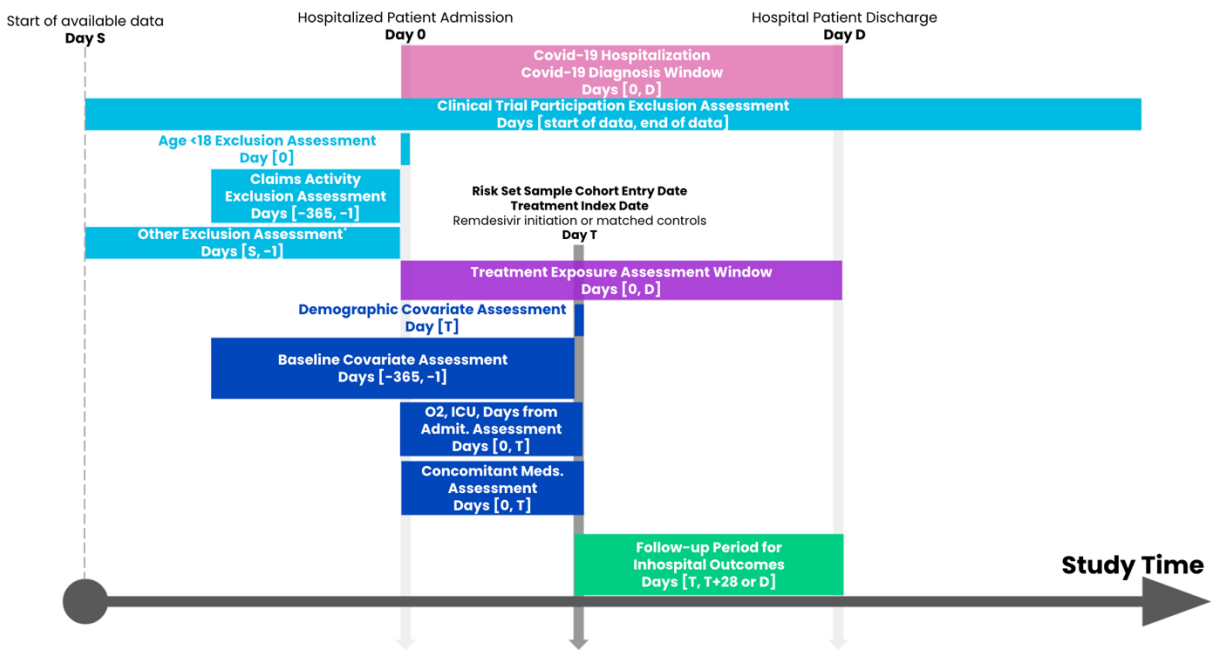
h Convalescent plasm defined as medical claims with procedures P9017, P9071, XW14325, P9099, XW13325 as well as Hospital Chargemaster Data

eTable 5. Distribution of Censoring Reasons by Treatment Status in the Initial-Treatment (IT) PS-Matched Cohort

Censor Reason	Remdesivir-Exposed	Referent	Overall
Discharge/end of hospitalization	20,121 (81.0%)	20,093 (80.8%)	40,214 (80.9%)
Max follow-up of 28 days	1,178 (4.7%)	988 (4.0%)	2,166 (4.4%)
Inpatient Mortality	3,557 (14.3%)	3,775 (15.2%)	7,332 (14.7%)

eTable 6. Distribution of Censoring Reasons by Treatment Status in the As-Treated (AT) PS-Matched Cohort

Censor Reason	Remdesivir-Exposed N (%)	Referent N (%)	Overall N (%)
Discharge/end of hospitalization	20,121 (81.0%)	15,335 (61.7%)	35,456 (71.3%)
Max follow-up of 28 days	1,178 (4.7%)	601 (2.4%)	1,779 (3.6%)
Inpatient Mortality	3,557 (14.3%)	2,661 (10.7%)	6,218 (12.5%)
Initiation of Remdesivir	0 (0%)	6,259 (25.2%)	6,259 (12.6%)



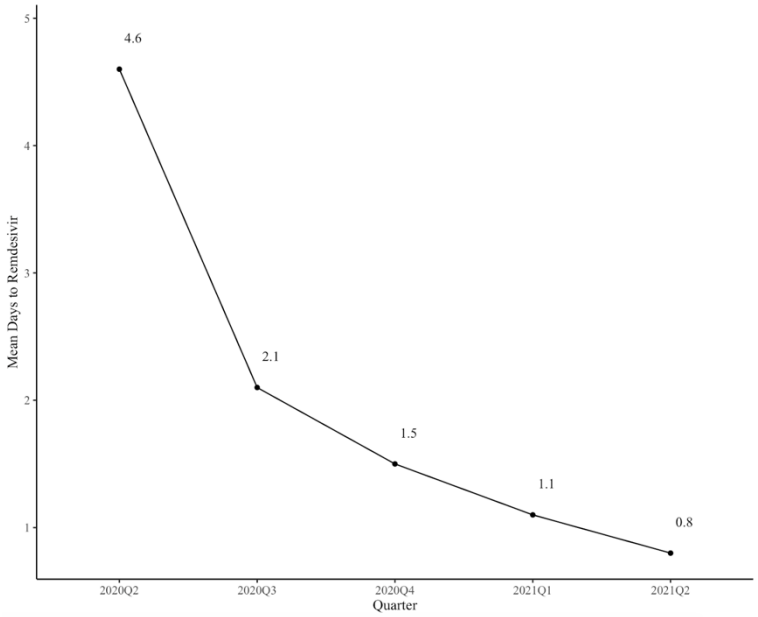
eFigure 1. Study Design. The study design diagram visually displays study design implementation and shows key temporal anchors (e.g., cohort entry date, exclusion assessment window, covariate assessment window, follow-up window) as described by Schneeweiss et al.[11] The vertical line represents the cohort entry dates (index dates), which is the first-order temporal anchor. Day S is the start of all available data in the database. Day 0 represents the patient's hospital admission date. Day T is the treatment index date. Day D is the hospital discharge date.
The boxes represent second-order temporal anchors (time windows) including the exclusion assessment to determine eligibility (light blue) and covariate assessment (dark blue). The green box represents the follow-up period starting from Day T.

The brackets in the boxes show time intervals anchored on Day 0 and Day T.

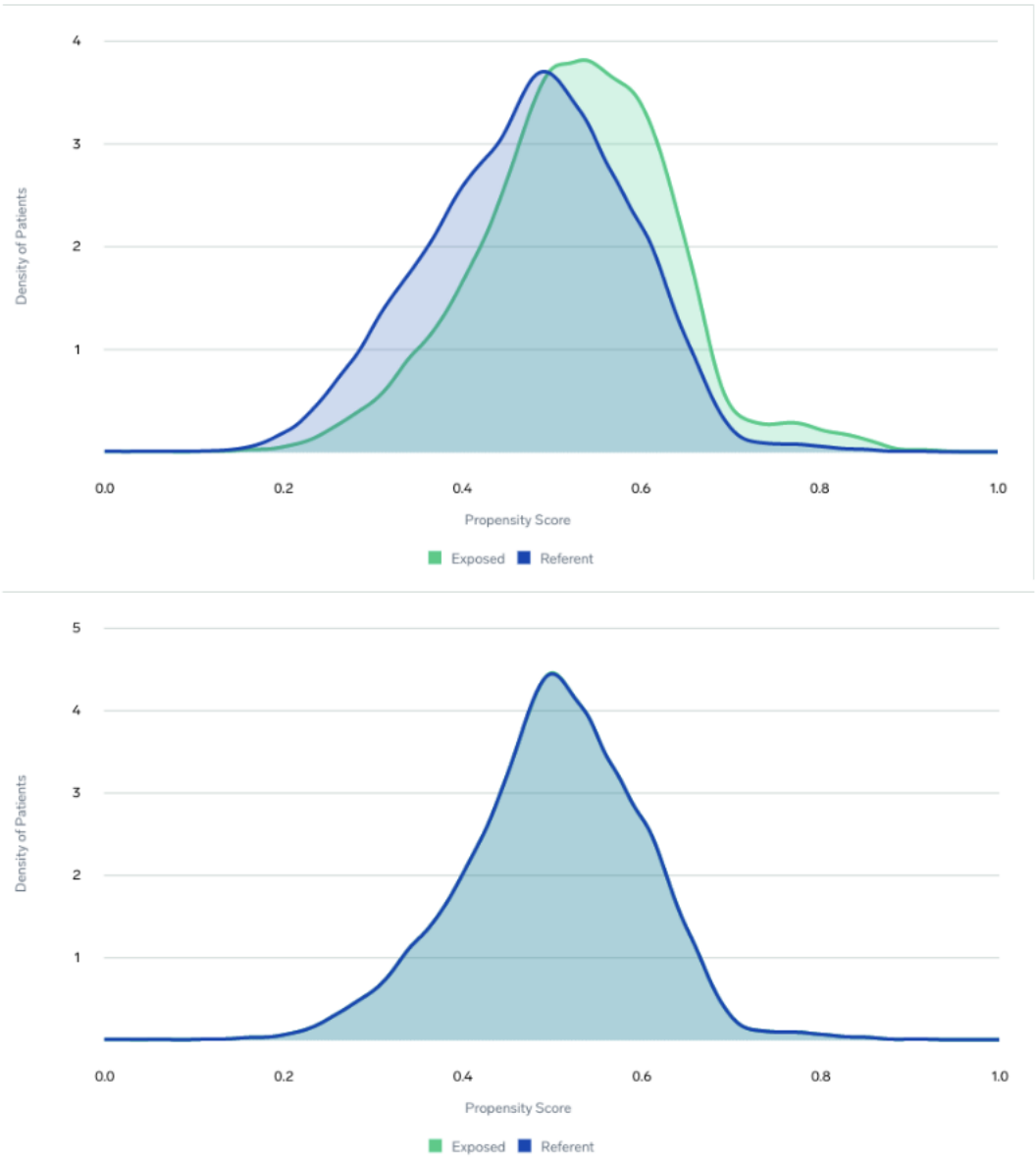
* Other exclusion assessment included remdesivir prior to hospitalization/EUA and prior Covid-19 hospitalization.

Abbreviations: ICU = intensive care unit; O2 = oxygen support

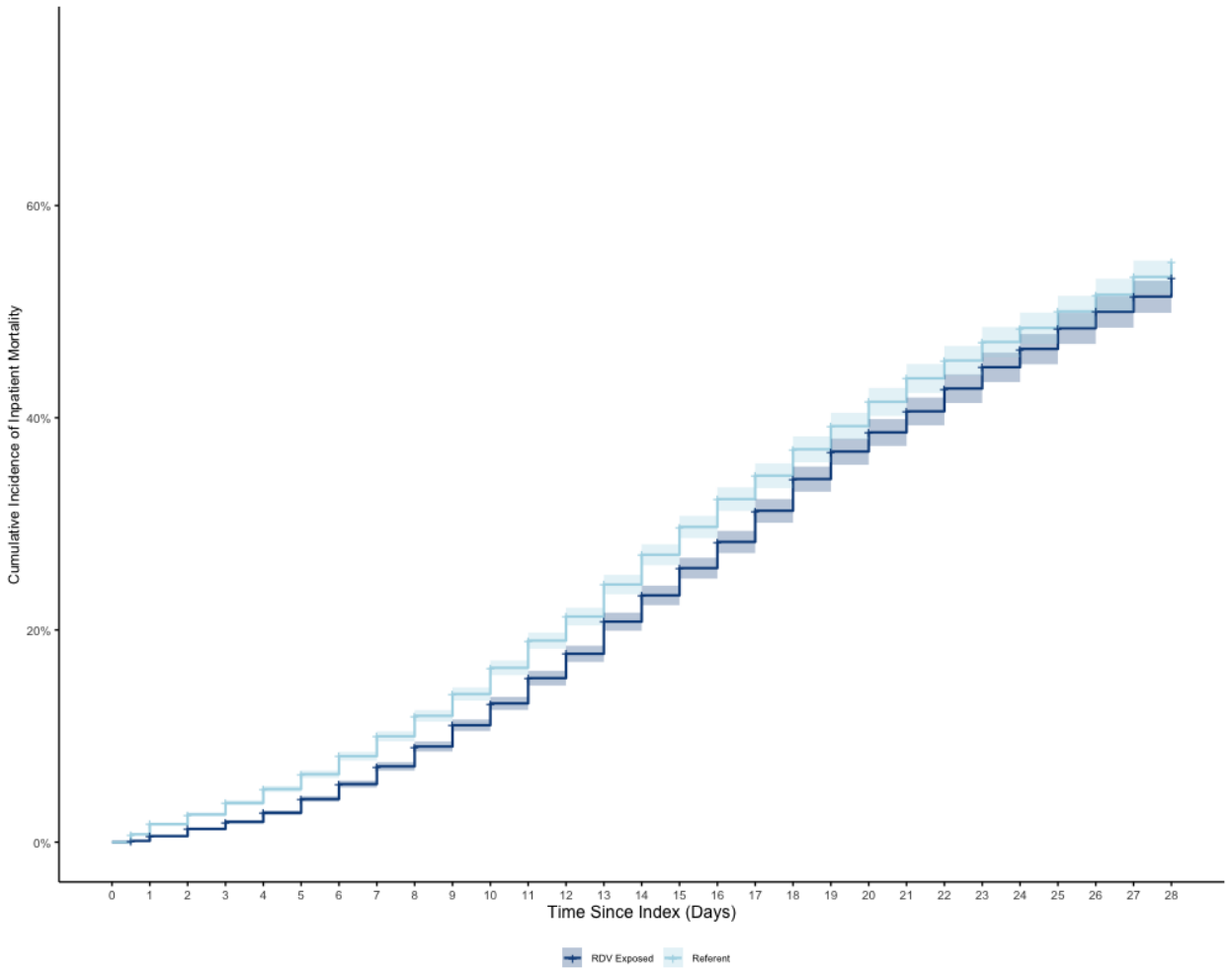
[11] Schneeweiss S, Rassen JA, Brown JS, Rothman KJ, Happe L, Arlett P, Dal Pan G, Goettsch W, Murk W, Wang SV. Graphical Depiction of Longitudinal Study Designs in Health Care Databases. Ann Intern Med. 2019 Mar 19;170(6):398-406. doi: 10.7326/M18-3079.



eFigure 2. Mean Days From Admission to Remdesivir Administration by Quarter Between 2020 and 2021

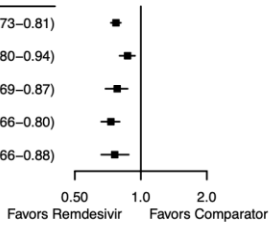


eFigure 3. Propensity Score Distribution Before and After PS-Matching



eFigure 4. Cumulative Incidence of Inpatient Mortality for Remdesivir-Exposed and Referent Control Patients. Note: In this figure, the cumulative incidence of mortality is estimated without accounting for the competing risk of hospital discharge or initiation of remdesivir.

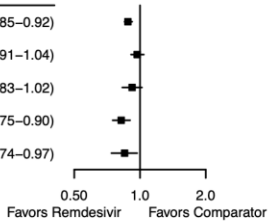
	Referent				Remdesivir				
Subgroups	Patients	Events	Person–Months	Rate (per PM)	Patients	Events	Person–Months	Rate (per PM)	HR (95% CI)
Overall	24,856	2,661	4,188	0.6	24,856	3,557	6,912	0.5	0.77 (0.73–0.81)
Room air	15,709	964	2,340	0.4	15,709	1,510	3,948	0.4	0.87 (0.80–0.94)
Low–flow	5,523	473	864	0.6	5,523	677	1,452	0.5	0.78 (0.69–0.87)
High–flow or NIV	2,646	811	696	1.2	2,646	884	1,032	0.9	0.73 (0.66–0.80)
ECMO/IMV	728	358	228	1.6	728	423	360	1.2	0.76 (0.66–0.88)



eFigure 5. Mortality by Oxygen Support Level Subgroup Using Cause-Specific Hazards Model (As-Treated). Control patients who crossed over to remdesivir were censored at the crossover date.

Abbreviations: CI = confidence interval; ECMO = extracorporeal membrane oxygenation; HR = hazard ratio; IMV = invasive mechanical ventilation; NIV = non-invasive ventilation; PM = person-months

	Referent				Remdesivir				
Subgroups	Patients	Events	Person–Months	Rate (per PM)	Patients	Events	Person–Months	Rate (per PM)	HR (95% CI)
Overall	24,856	3,775	6,066	0.6	24,856	3,557	6,908	0.5	0.88 (0.85–0.92)
Room air	15,709	1,553	3,488	0.4	15,709	1,510	3,953	0.4	0.97 (0.91–1.04)
Low–flow	5,523	725	1,292	0.6	5,523	677	1,457	0.5	0.92 (0.83–1.02)
High–flow or NIV	2,646	1,007	910	1.1	2,646	884	1,026	0.9	0.82 (0.75–0.90)
ECMO/IMV	728	450	318	1.4	728	423	359	1.2	0.85 (0.74–0.97)



eFigure 6. Mortality by Oxygen Support Level Subgroup Using Fine-Gray Subdistribution Hazard Model (Initial-Treatment). Patients were censored on the earliest occurrence of discharge to home, inpatient death, maximum follow-up of 28 days.

Abbreviations: CI = confidence interval; ECMO = extracorporeal membrane oxygenation; HR = hazard ratio; IMV = invasive mechanical ventilation; NIV = non-invasive ventilation; PM = person-months