

# Remdesivir is associated with decreased mortality in hospitalised COVID-19 patients requiring high-flow oxygen in the United States

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# Key Findings

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- In routine clinical practice setting, **remdesivir is associated with reduced mortality** regardless of supplemental oxygen requirements upon admission
- This clear and consistent benefit was observed across **all dominant variant periods** from December 2020 to April 2022

# Objective of the study

- To compare inpatient all-cause mortality in patients who were administered remdesivir (RDV) in the first two days of hospitalization to patients vs. those not administered remdesivir during hospitalization among patients hospitalized **with COVID-19 as a primary discharge diagnosis and receiving high-flow oxygen/non-invasive ventilation upon admission**
  - Endpoints were examined according to timing of COVID-19 hospitalization in **different variants of concern (VOC) periods**: pre-Delta (December 2020-April 2021), Delta (May 2021-November 2021) and Omicron (December 2021- April 2022)
  - Endpoints were also examined among patients receiving **no supplementary oxygen, low-flow oxygen and invasive mechanical ventilation/ECMO upon admission**
- **Primary endpoints:**
  - 14-day in-hospital mortality
  - 28-day in-hospital mortality

# Study Design

## Comparative effectiveness study using PINC AI Healthcare Database

- Data source: hospital billing database covering ~25% of all US hospitalizations from 48 states
- All baseline variables are examined within the first two days of hospitalization

Inclusion criteria	✓	First admission to the hospital Dec 1, 2020-Apr 30, 2022
	✓	Age ≥18 years old
	✓	<b><u>Primary</u> discharge diagnosis of COVID-19</b> (ICD-10-CM: U07.1) flagged as “present-on-admission”
Exclusion criteria	×	Pregnant
	×	Had incomplete /erroneous data fields
	×	Transferred from another hospital or hospice
	×	Transferred to another hospital
	×	Admitted for elective procedures
	×	Discharged or died during the baseline period (first two days of <u>hospitalization</u> )

RDV

Non-RDV

Treatment

RDV treatment within 2 days of admission

Patients not receiving RDV during the hospitalization

- **Primary Endpoints:** 14-day and 28-day all-cause inpatient mortality (discharge status of “expired” or “hospice”)
- **VOC periods:** Pre-Delta (Dec 2020-Apr 2021), Delta (May-Nov 2021), Omicron (Dec 2021-Apr 2022)

# Methodology published previously in peer-reviewed journals

*Clinical Infectious Diseases*

MAJOR ARTICLE



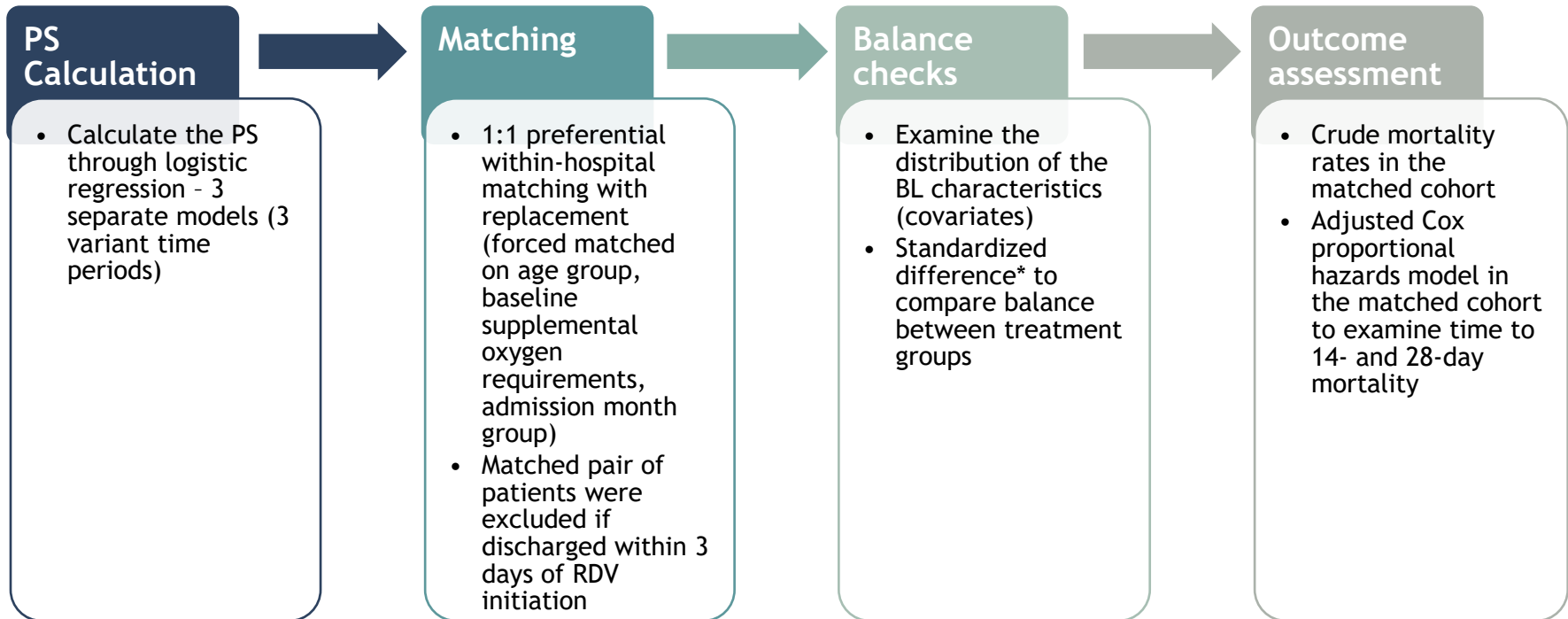
## Remdesivir Treatment in Hospitalized Patients With Coronavirus Disease 2019 (COVID-19): A Comparative Analysis of In-hospital All-cause Mortality in a Large Multicenter Observational Cohort

Essy Mozaffari,<sup>1</sup> Aastha Chandak,<sup>2,✉</sup> Zhiji Zhang,<sup>2</sup> Shuting Liang,<sup>1</sup> Mark Thrun,<sup>1</sup> Robert L. Gottlieb,<sup>3,4,5,6,✉</sup> Daniel R. Kuritzkes,<sup>7</sup> Paul E. Sax,<sup>8</sup> David A. Wohl,<sup>9</sup> Roman Casciano,<sup>2,✉</sup> Paul Hodgkins,<sup>1</sup> and Richard Haubrich<sup>1</sup>

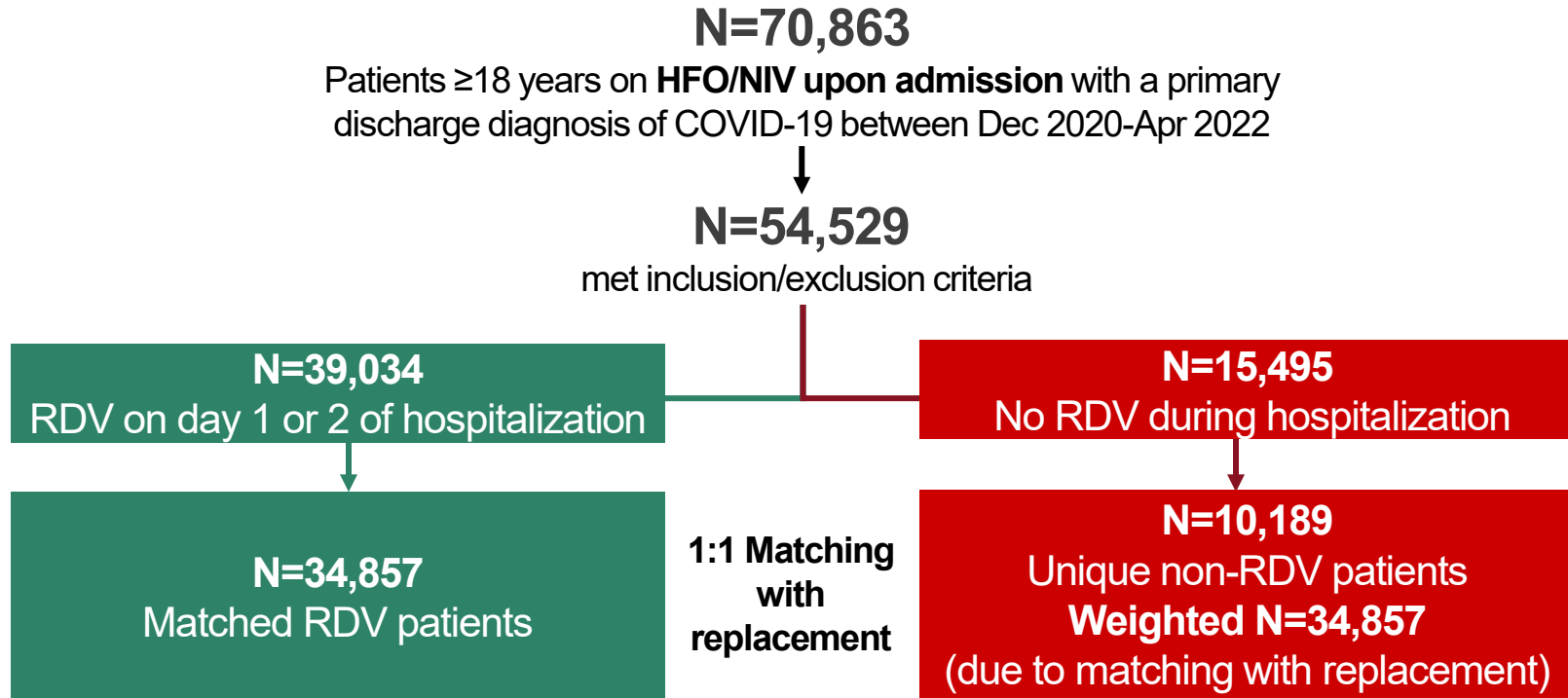
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# Statistical analysis approach

Propensity score (PS) matching approach was used to balance the two groups



# Study cohort

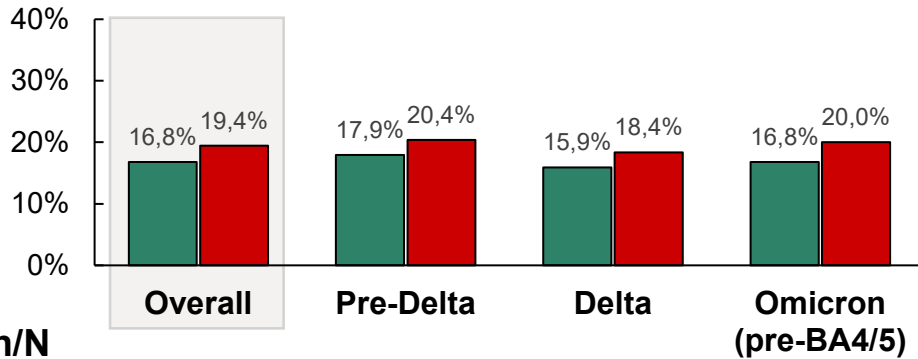


# Unadjusted analysis

Among patients on HFO/NIV upon admission, mortality rates were significantly lower for RDV vs. non-RDV across all variant periods

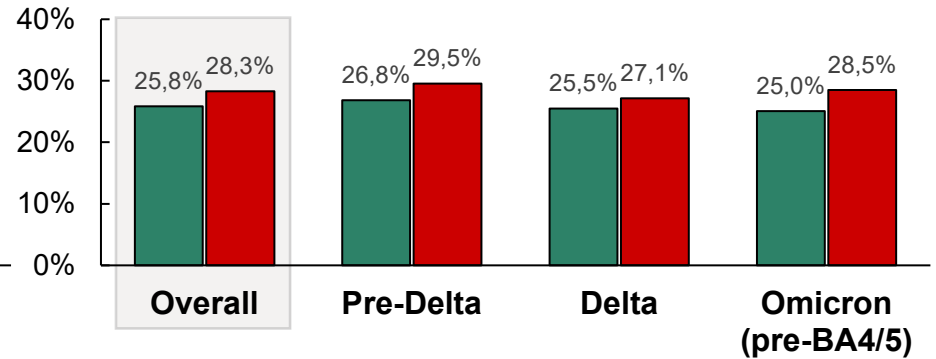
## 14-day mortality

■ RDV ■ Non-RDV



## 28-day mortality

■ RDV ■ Non-RDV



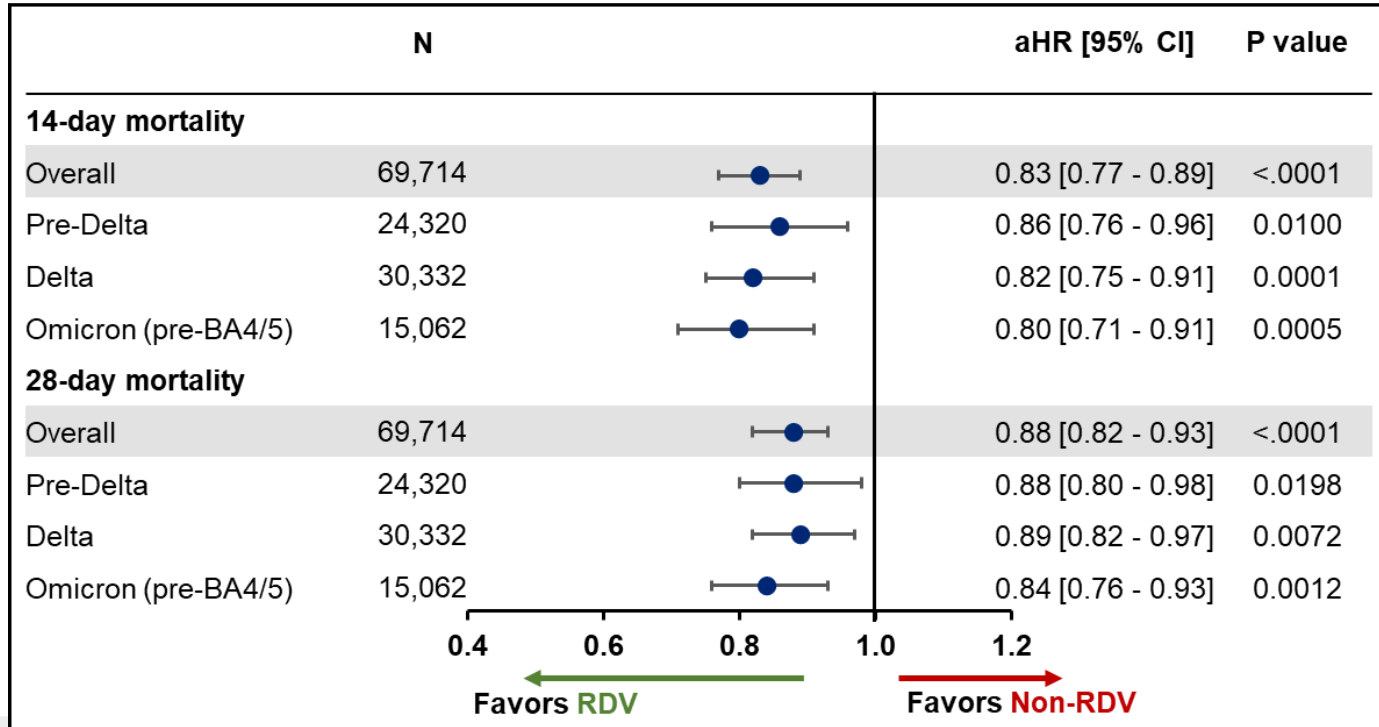
n/N	Overall	Pre-Delta	Delta	Omicron (pre-BA4/5)
<b>RDV</b>	<b>5,853/34,857</b>	<b>2,180/12,160</b>	<b>2,409/15,166</b>	<b>1,264/7,531</b>
<b>Non-RDV</b>	<b>6,770/34,857</b>	<b>2,478/12,160</b>	<b>2,783/15,166</b>	<b>1,509/7,531</b>

n/N	Overall	Pre-Delta	Delta	Omicron (pre-BA4/5)
<b>RDV</b>	<b>9,009/34,857</b>	<b>3,260/12,160</b>	<b>3,863/15,166</b>	<b>1,886/7,531</b>
<b>Non-RDV</b>	<b>9,853/34,857</b>	<b>3,591/12,160</b>	<b>4,115/15,166</b>	<b>2,147/7,531</b>



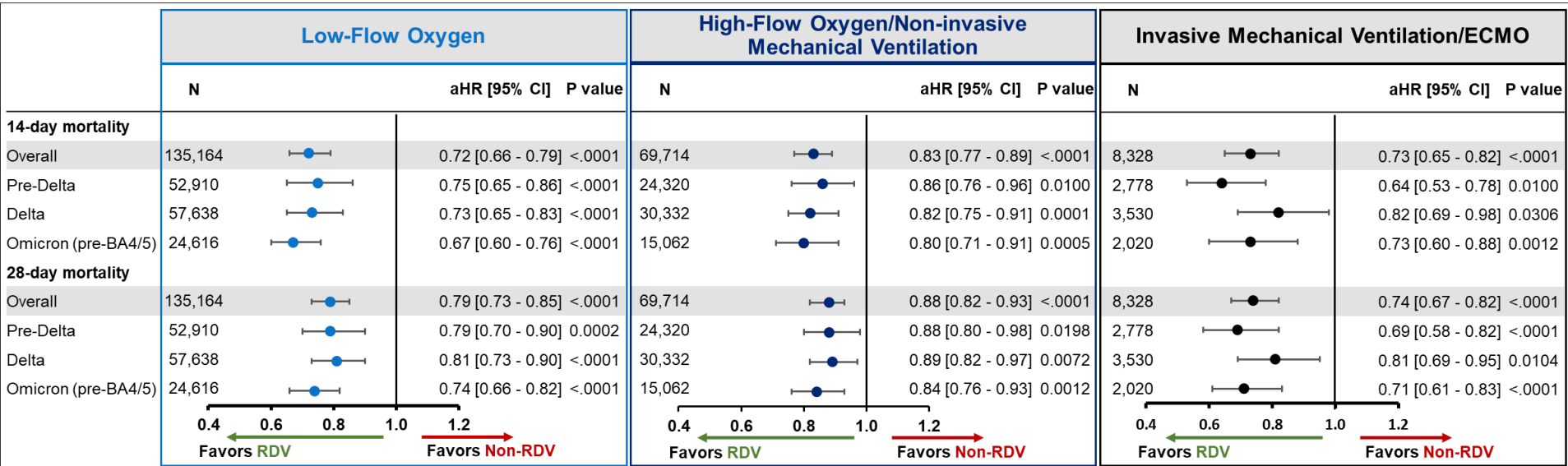
# Adjusted analysis

Among patients on HFO/NIV upon admission, RDV had significantly lower mortality risk compared to non-RDV across all VOC periods



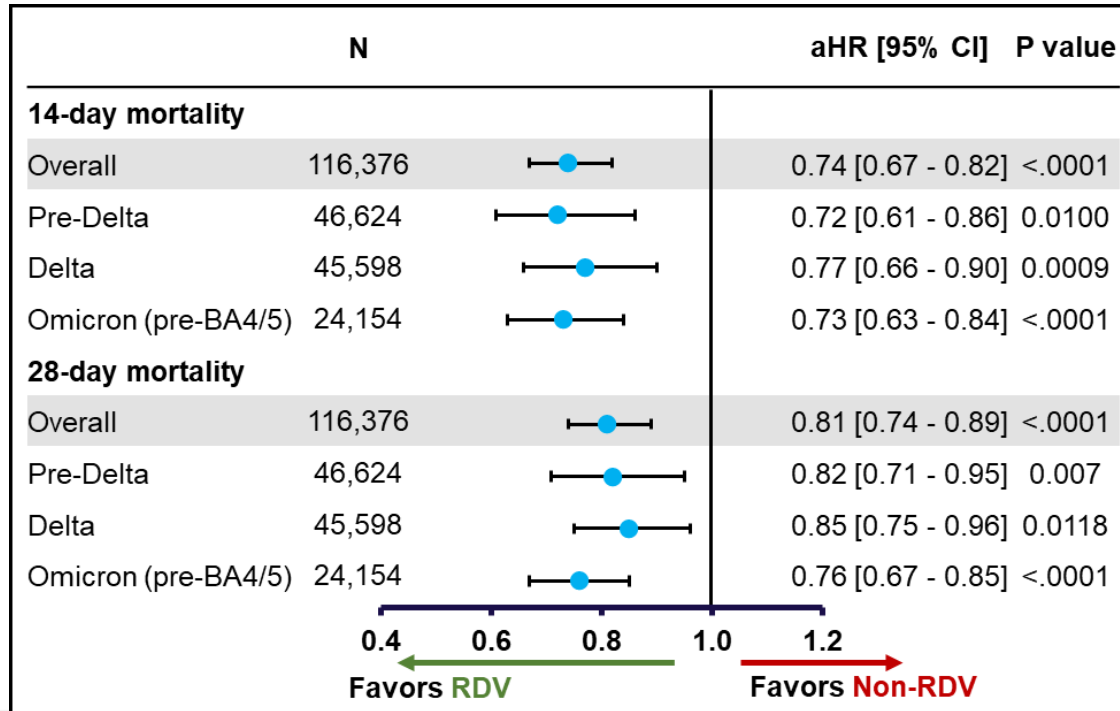
# Adjusted analysis

## Consistent mortality reduction with RDV observed for all levels of supplemental oxygenation requirements across all VOC periods



# Adjusted analysis

**RDV also showed a consistent benefit among patients not reporting supplementary oxygen upon admission**



# Conclusions

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- Using a large cohort of hospitalized COVID-19 patients in routine clinical practice, this study demonstrated that the **initiation of RDV upon admission leads to statistically significant reduction in mortality** across all variant periods studied (through April 2022)
- Given the **high mortality rates in severely or critically ill COVID-19 patients** across emerging variants, **use of remdesivir in this population could be life-saving**
- While the initiation of antivirals early in the disease course is clearly optimal to decrease risk of inflammatory dysregulation, there are still benefits of reduction in mortality **when initiated in patients presenting later in the disease course**

# Poster Presentations

Focusing on effectiveness of remdesivir in immunocompromised and cancer patients

Poster#	Poster title	Date	Timing
<b>LB#074</b>	Remdesivir is associated with lower mortality in cancer patients hospitalized for COVID-19 across emerging variants	<b>Tuesday, April 18, 2023</b>	<b>12:00- 13:30pm</b>
<b>LB#081</b>	Immunocompromised patients hospitalized for COVID-19 in the United States: evolving patient characteristics and clinical outcomes across emerging variants		

# Questions?



# Statistical Analysis: PS calculation

PS calculation

Matching

Baseline check/diagnostics

Outcome assessment

## Key covariates used in PS calculation

- **Baseline demographics:** age, gender, race, ethnicity, primary payor
- **Key comorbidities:** obesity, COPD, diabetes, renal disease, cardiovascular disease, cancer, immunocompromised condition
- **Hospital characteristics:** bed size, urban/rural, teaching, region of the hospital
- **Admission month**
- **Admission from SNF**
- **ICU/General ward** at baseline
- **Severity level** identified through level of oxygenation used at baseline
- **Other indicators of severity** based on admit diagnoses (respiratory failure, hypoxemia, sepsis, pneumonia)
- **Concomitant medications** at baseline: corticosteroids, convalescent plasma, anticoagulants, tocilizumab, baricitinib

Baseline=Day 1 or 2 of hospitalization

Patients that died/discharged during the baseline period are excluded

# Statistical Analysis: Matching

PS calculation

Matching

Baseline check/diagnostics

Outcome assessment

## 1:1 Preferential Same-Hospital Matching with replacement

1 PS-matching (caliper=0.2x s.d. of the logit of the PS) for patients with same age group, same supplemental oxygenation, same two/three-month blocks of admission month **within the same hospital**

↓ If unmatched in step 1

2 PS-matching (caliper=0.2x s.d. of the logit of the PS) for patients with same age group, same supplemental oxygenation, same two/three-month blocks of admission month **within another RDV-using hospital of same bed size**

Matched patients were not discharged within 3 days of RDV initiation to emulate ACTT-1 exclusion (which excludes anticipated discharges/transfers within 72 hrs)

**Matching with replacement:** allowed for majority of the patients treated with RDV to be matched and included in the analysis despite a restricted matching criteria and higher % of RDV use in the study cohort; hence conclusions made are applicable to majority of the RDV patients



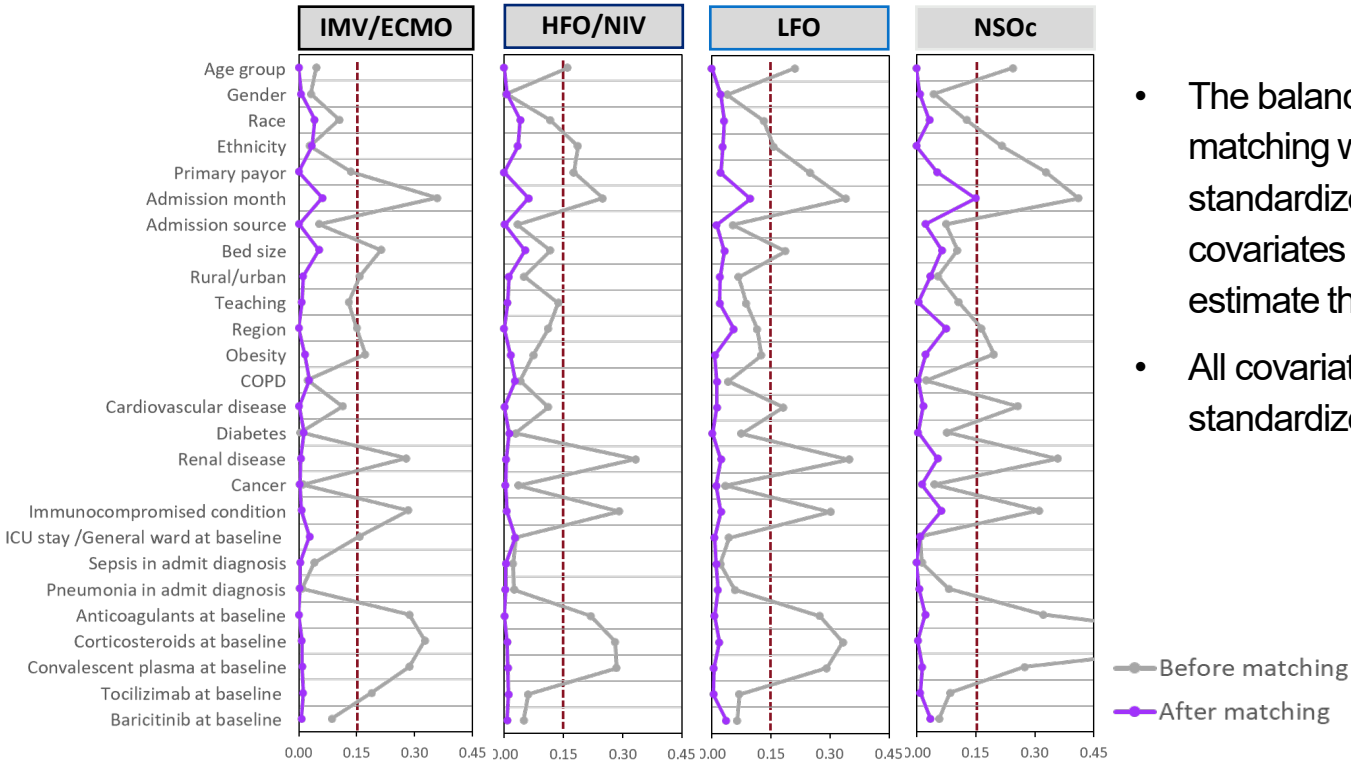
# Statistical Analysis: Baseline check/diagnostics

PS calculation

Matching

Baseline check/diagnostics

Outcome assessment



- The balance in the covariates after matching was verified by the absolute standardized differences of the covariates included in the model to estimate the propensity scores
- All covariates had an absolute standardized difference value of  $<0.15$

# Statistical Analysis: Outcome assessment

PS calculation

Matching

Baseline check/diagnostics

Outcome assessment

## — Time to mortality outcome: Cox Proportional Hazards Model

- **Mortality:** discharge status of “expired” or “hospice”
  - **Event of interest:** Time to 14-day and 28-day mortality after baseline period
  - **Healthy discharge:** patients who were discharged before the 14-day or 28-day time period were censored at the 14-day and 28-day time points
- A marginal model to account for hospital-level cluster effects was used
- The following variables were adjusted for in the outcomes analyses models:
- Age (continuous)
  - Admission month
  - Anticoagulants use at baseline
  - Convalescent plasma at baseline
  - Steroids use at baseline
  - Tocilizumab use at baseline
  - Baricitinib at baseline
  - Hospital ward upon admission (general ward vs. ICU unit)