The Impact of COVID-19 Treatments on Patient Outcomes: A Probabilistic View

00637

Bradley S. Price[1], Maryam Khodaverdi[1], Hamidreza Moradi[2], H. Timothy Bunnnell[3], James Z. Porterfield[4], Michael T. Vest[5], Susan L. Santangelo[6], Wesley Kimble[1], Alfred J. Anzalone[7], Jeremy Harper[8], Sally L. Hodder[1]
[1]West Virginia Clinical and Translational Science Institute, Morgantown, WV, United States, [2]University of Mississippi Medical Center, Jackson, MS, United States, [3]Nemour's Children's Health, Wilmington, DE, [4]University of Kentucky, Lexington, KY, United States, [5]Christiana Care Health System, Newark, USA, [6]Tufts University, Boston, MA, United States, [7]University of Nebraska Medical Center, Omaha, NE, United States, [8]Owl Health Works LLC, Indianapolis, IN

BACKGROUND

Efficacy and safety of various COVID-19 treatments have usually been studied with prospective, randomized clinical trials (RCT). However, the limited sample sizes of RCTs often limit their utility, especially for subsets of patients. Retrospective analyses using very large datasets enable investigation of various therapeutic outcomes among patients with differing levels of disease severity.

OBJECTIVE

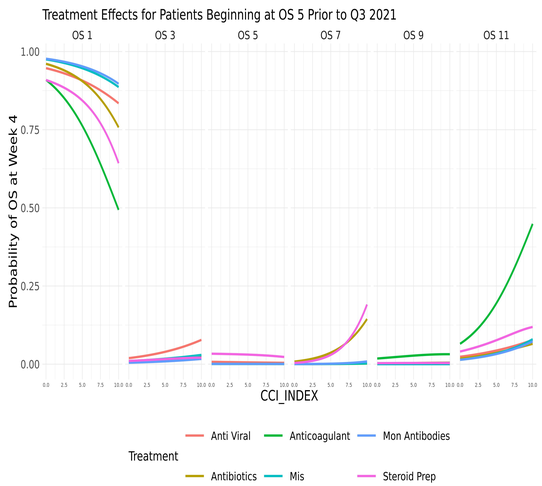
- ***This study seeks to find the best therapy or combination of therapeutic agents for subsets of patients with various levels of COVID-19 disease severity***.

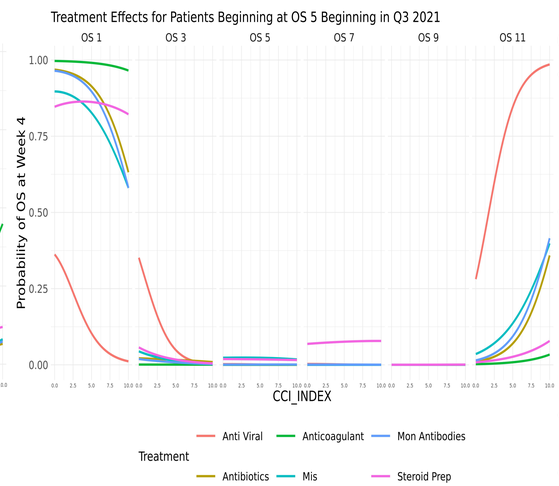
METHODS

- Using the National COVID Cohort Collaborative (N3C), containing data on 3,756,433 SARS-CoV-2 infected persons from 69 centers across the United States, disease severity was defined using a 6-level ordinal scale (OS) (Table 1).
- Baseline OS for each patient was defined as the maximum OS level that occurred in the first 7 days (Week 1) after COVID-19 diagnosis.
- Outcome is the probability of moving from a higher OS level (more sever disease) to Level 1 (outpatient) at week 4
- The Charlson Co-morbidity Index (CCI) was used to the measure the number of co-morbidities
- Age>60 years, ethnicity, quarter of diagnosis, and treatments are independent variables (data not shown).
- Treatment categories include anti-coagulants (AC), steroids, antibiotics, antivirals (AV), monoclonal antibodies (MA), and a miscellaneous group that included all other treatments.
- Data were collected from Q2 2020 to Q4 2021 and stratified by before and after Q3 2021 to investigate the effect of the Delta variant. At the time of analysis, there are very limited data on the Omicron variant, as pooled data is aggregated from all sites
- For OS 3 and OS 5, we assumed that all patients were treated with MA. Similarly, for OS 7 and 9 we assume that steroids were given.
- Elastic Net Penalized Multinomial Logistic Regression was used to obtain probabilities of treatment effects compared to OS.

Table 1: Summary table of definitions of the Ordinal Scale, pre and post Delta results of our analysis, and the best treatment combinations recommendation based on analysis from discharge at Day 28.

		Pre-Delta (Q2 2020 to Q2 2021)		Post-Delta (Q3-2021-Q4 2021)	
Baseline Ordinal Scale (OS) Level	**Ordinal Scale Description**	**Week 1 Sample Size**	**Rx with Highest Probability of Hospital Discharge at 28 Days**	**Week 1 Sample Size**	**Rx with Highest Probability of Hospital Discharge at 28 Days**
OS 1	Outpatient				
OS 3	Hospitalized	105401	Antivirals with Monoclonal Antibodies	49537	Antivirals with Monoclonal Antibodies
OS 5	Hospitalized with Oxygen	11622	Monoclonal Antibodies Only	2804	Anticoagulant with Monoclonal Antibodies
OS 7	Hospitalized on Ventilator	9662	Low CCI: Steroids and Antibiotics High CCI: Steroids Only	1277	Low CCI: Steroids and Anticoagulants High CCI: Steroids and Antibiotics
OS 9	Hospitalized on ECMO or Vasopressors	14885	Low CCI: Steroids with Monoclonal Antibodies High CCI: Steroids with Monoclonal Antibodies	4229	Low CCI: Steroids with Monoclonal Antibodies Any CCI: Steroids with Antivirals
OS 11	Death	7514			

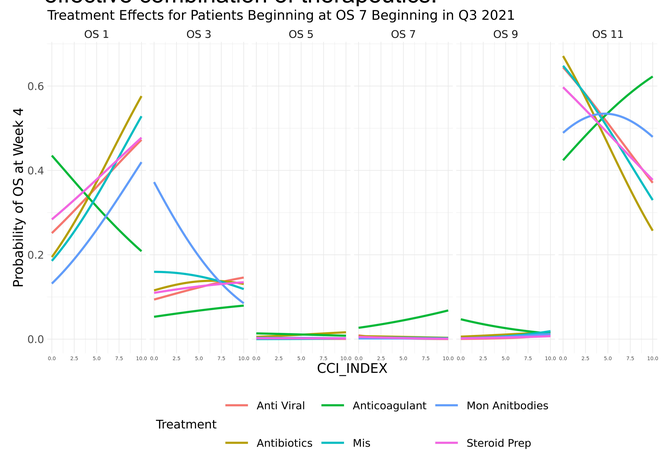




The project described was supported by the National Institutes of Health, U54GM104942-05S2, U54GM104941, U54GM115516, U54 GM115458, The analyses described in publication were conducted with data or tools accessed through the NCATS N3C Data Enclave supported by NCATS U24 TR002306. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

RESULTS

- Across all baseline OS levels, no one standard combination of treatments provides the highest probability of hospital discharge at Week 4 (Table 1).
- Being male and older than age 60 years are associated with lower probabilities of hospital discharge by Week 4.
- Higher CCI is associated with a higher probability of death by Day 28 and lower CCI values lead to a higher probability of hospital discharge, except for those starting at OS Level 7.
- Variants (Delta vs previous variants) influence the most effective combination of therapeutics.



CONCLUSIONS

- These data suggest that optimal therapeutic agent choice may be guided by the level of disease severity and presence of specific SARS-CoV-2 variant.
- The assessed treatment regimes confirmed previously identified efficacious treatments, e.g., steroids and MA, but also suggest the potential for positive impact of other treatments combinations.

LIMITATIONS

- As this is a retrospective analysis, therefore, unrecognized confounding may be present.
- Demonstrated associations may not be causal. However, unlike RCTs, use of very large datasets such as N3C enables investigation of optimal treatments for subsets of patients defined by disease severity.