Cost of Long Covid Following Severe Disease – A US Healthcare Database Analysis

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Introduction

- The United Kingdom National Health Services describes Ongoing COVID-19 Symptoms (OCS) and Post-COVID-19 Syndrome (PCS) as the persistence of COVID-19 symptoms beyond 4- and 12 weeks, respectively.[1]
- Costs and predictors for OCS and PCS following COVID-19 infection are not known.

Objective

- Our study was designed to evaluate healthcare costs associated with OCS and PCS in patients with severe or critical COVID-19 disease from the perspective of the US payers and develop machine models to predict patients at risk for high cost of care.

Methods

- Database: IBM® MarketScan® Commercial and Medicare Supplemental databases
- Patients with COVID-19 (first date = index) from April 1, 2020 to June 30, 2021 were stratified by severity (mild, moderate and severe/critical (SC)), based on the Janssen Phase 3 ENSEMBLE Clinical Trial definition of severity.[2] Only SC patients were included in this study.
- Duration of disease was defined as follows: from 5 days before positive test to last related visit/prescription, with a maximum gap of 35 days between visits/prescriptions.
  - OCS was defined as duration of disease 4 to 12 weeks
  - PCS was defined as duration of disease exceeding 12 weeks
- Variables included demographics, comorbidities (Elixhauser index (EI) and all 31 Elixhauser disease domains), and all COVID-19 signs and symptoms (CSS) during index disease, as well as treatments received during the inpatient care.
- All cost of care for the entire duration of the disease were estimated for each patient. Two types of costs were calculated:
  - All-cause costs (any diagnoses)
  - Disease-specific costs (only CSS diagnoses)
- Predictive modeling was done using the DataRobot Platform. 62 machine learning algorithms were evaluated. An Ensemble model (Blender) was generated, using the best available algorithms. The purpose of the Ensemble model was to maximize model accuracy (vs speed).

Results

- A total of 34,317 patients were analyzed. The characteristics of the patient population, and key associated variables, are shown in Table 1.

Table 1: Patient Population with some of the key variables used for modeling

	No PCS	PCS
N	27,628	6,689
Age (mean (standard deviation (SD))	54.73 (14.63)	59.09 (15.35)
Female (vs Male)	12,099 (43.8%)	3,135 (46.9%)
Payer = Medicare (%)	4,899 (17.7%)	1,913 (28.6%)
Elixhauser Index (mean (SD))	1.96 (2.17)	2.98 (2.84)
Functional Comorbidity Index (mean (SD))	2.01 (1.96)	2.81 (2.29)
Comorbidities		
Cardiac Arrhythmia	2,761 (10.0%)	1,172 (17.5%)
Peripheral vascular disorders	1,409 (5.1%)	682 (10.2%)
Hypertension Uncomplicated	12,063 (43.7%)	3,592 (53.7%)
Hypertension Complicated	2,206 (8.0%)	1,005 (15.0%)
Chronic pulmonary disease	3,280 (11.9%)	1,375 (20.6%)
Diabetes Uncomplicated	5,850 (21.2%)	1,781 (26.6%)
Diabetes Complicated	4,858 (17.6%)	1,629 (24.4%)
Obesity	4,974 (18.0%)	1,510 (22.6%)
COVID-19 Signs and Symptoms		
Sepsis	6,325 (22.9%)	2,219 (33.2%)
Shortness of Breath	24,461 (88.5%)	6,198 (92.7%)
Sore Throat	4,233 (15.3%)	1,591 (23.8%)
Hypoxemia	11,804 (42.7%)	3,481 (52.0%)
Tachycardia	4,688 (17.0%)	1,736 (26.0%)
Fatigue	3,389 (12.3%)	1,155 (17.3%)
Cough	11,902 (43.1%)	3,136 (46.9%)
Fever	8,378 (30.3%)	2,304 (34.4%)
Malaise	8,011 (29.0%)	3,187 (47.6%)
Chest Pain	8,426 (30.5%)	2,636 (39.4%)
Gastrointestinal symptoms	6,810 (24.6%)	2,203 (32.9%)
Confusion	3,131 (11.3%)	1,511 (22.6%)
Thrombosis	810 (2.9%)	542 (8.1%)
Pneumonia	21,901 (79.3%)	5,743 (85.9%)
Acute Respiratory Failure	20,947 (75.8%)	5,409 (80.9%)
COVID-19 Associated Treatments		
additional inpatient admission	17,232 (62.4%)	5,152 (77.0%)
ICU admission	8,822 (31.9%)	3,110 (46.5%)
Mechanical Ventilation	1,005 (3.6%)	884 (13.2%)
Non-Mechanical Ventilation	1,175 (4.3%)	650 (9.7%)
Corticosteroid Injection	3,599 (13.0%)	1,170 (17.5%)
Remdesivir	10,249 (37.1%)	2,369 (35.4%)
Platelet	3,722 (13.5%)	1,022 (15.3%)
Plasma	328 (1.2%)	82 (1.2%)
Bamlanivimab	66 (0.2%)	19 (0.3%)
Dexamethasone	362 (1.3%)	69 (1.0%)
Betamethasone	163 (0.6%)	99 (1.5%)
Albuterol	373 (1.4%)	194 (2.9%)
ECMO	30 (0.1%)	57 (0.9%)

*PCS: Post-COVID-19 Syndrome

- Analyses of all-cause and disease-specific costs, by payer and duration of disease, are shown for all SC patients in Table 2.

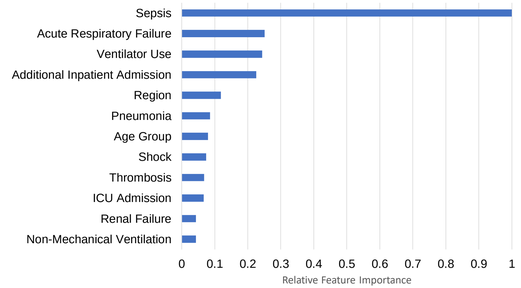
Table 2: Disease-specific and all-cause costs in COVID-19 SC patients, by disease duration and payer. Mean costs (95% confidence intervals)

	COMMERCIAL	MEDICARE
Disease Specific Costs Only		
Duration of disease < 4 weeks	$17,333 (95%CI:$16,485-$18,181)	$5,393 (95%CI:$4,917-$5,870)
OCS	$27,043 (95%CI:$25,711-$28,376)	$10,511 (95%CI:$9,752-$11,271)
PCS	$68,069 (95%CI:$62,739-$73,400)	$25,518 (95%CI:$23,179-$27,857)
Disease Specific Incremental payments		
From duration of disease < 4 weeks to OCS	$9,711 (95%CI:$8,133-$11,288)	$5,118 (95%CI:$4,226-$6,011)
From duration of disease < 4 weeks to PCS	$50,736 (95%CI:$45,337-$56,136)	$20,124 (95%CI:$17,742-$22,507)
All Healthcare Costs		
Duration of disease < 4 weeks	$31,255 (95%CI:$30,205-$32,305)	$16,484 (95%CI:$15,801-$17,167)
OCS	$49,866 (95%CI:$48,181-$51,550)	$29,457 (95%CI:$28,458-$30,457)
PCS	$126,094 (95%CI:$119,373-$132,814)	$64,520 (95%CI:$61,772-$67,267)
All Healthcare Incremental payments		
From duration of disease < 4 weeks to OCS	$18,611 (95%CI:$16,635-$20,586)	$12,973 (95%CI:$11,766-$14,180)
From duration of disease < 4 weeks to PCS	$94,839 (95%CI:$88,029-$101,649)	$48,036 (95%CI:$45,199-$50,872)

*SC: Severe/Critical, OCS: Ongoing COVID-19 Symptoms, PCS: Post-COVID-19 Syndrome

- For predictive modeling: highest accuracy was obtained from a generalized linear model (GLM) Blender with gamma distribution. The gamma deviance for the GLM Blender were as follows: cross-validation: 1.2067; holdout: 1.2241; validation: 1.1959. This model took predictions from 3 different algorithms, selected from 62 distinct models. Key predictors of cost are shown in Figure 1 and included sepsis and acute respiratory failure.

Figure 1: Top 12 Feature impact on GLM blender model. Sepsis was the most predictive variable for cost



Key Findings

- **In patients with severe or critical COVID-19, Post-COVID-19 Syndrome resulted in:**
  - **An increase in all-cause and disease-specific costs for commercial payers of $94,839 (95%CI:$88,029-$101,649) and $50,736 (95%CI:$45,337-$56,136), respectively, per patient.**
  - **An increase in all-cause and disease-specific costs for Medicare of $48,036 (95%CI:$45,199-$50,872) and $20,124 (95%CI:$17,742-$22,507), respectively, per patient.**
  - **As expected, Medicare costs are much lower than costs for commercial payers.**
- **A predictive model identified sepsis, ventilator use and acute respiratory failure within the top 12 predictors of costs.**

Conclusions

- **Post-COVID-19 Syndrome more than triples the cost of treating COVID-19 in severe or critical patients.**
- **Predicting patients at high risk for Post-COVID-19 Syndrome may help with healthcare resource allocation and cost containment.**

References:

1. https://www.nhs.uk/conditions/coronavirus-covid-19/long-term-effects-of-coronavirus-long-covid/ - Last accessed 04/04/2022
2. https://www.jnj.com/coronavirus/ensemble-1-study-protocol - Last accessed 04/04/2022

Abbreviations:

COVID-19: Coronavirus disease 2019
ECMO: Extracorporeal membrane oxygenation
GLM: Generalized linear model
ICU: Intensive Care Unit
OCS: Ongoing COVID-19 Symptoms
PCS: Post-COVID-19 Syndrome
SC: Severe/Critical
SD: Standard deviation

ISPOR – May 15-18, 2022

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