

Duration of COVID-19 and Predictors for Long COVID – A US Healthcare Database Analysis

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Introduction

- The Coronavirus disease (COVID-19 presents different clinical manifestations, ranging from complete absence of symptoms to critical illness.
 - The US National Institutes of Health (NIH) defines the following categories of severity among adults with COVID-19: asymptomatic, mild, moderate, severe, and critical illness.¹
 - Comparable categorization of COVID-19 severity have also been developed and used in the Janssen Phase 3 Ensemble vaccine clinical trial.²
- The average course of COVID-19 has been reported between 2 and 6 weeks. Some patients, however, exhibit symptoms for weeks or months following the acute stage of the illness. The United Kingdom National Health Service (NHS) thus defines long covid as: ongoing symptomatic covid (OSC), in patients with symptoms that extend for 4 to 12 weeks, and post-COVID-19 Syndrome (PCS), for patients with ongoing symptoms for more than 12 weeks.³

Objective

- Analyze the duration of disease in patients with mild, moderate and severe/critical disease, and assess the percentage of patients at risk for PCS in each category.

Methods

- Study Design:** Retrospective database analysis in IBM® MarketScan® Commercial and Medicare Supplemental databases, of patients with COVID-19, from April 1, 2020 to June 30, 2021.
- Variables** included demographics, comorbidities (Elixhauser index (ECI) 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.
- Disease Severity:** All patients were stratified by severity of disease (mild, moderate and severe/critical (SC)), based on the Janssen Phase 3 ENSEMBLE Clinical Trial definition of severity.²
- 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.
- Statistical Analyses:** Descriptive statistics were reported for all study variables based on severity of disease— means and standard deviations for continuous variables, frequencies and percentages for categorical variables. Generalized linear models (GLM) were built to evaluate duration of disease, and logistic regression analyses were conducted to identify risk factors for PCS across all COVID-19 patients and within each severity group.

Results

- The study included 383,883 patients with a COVID-19 diagnosis, including 160,326 mild, 189,240 moderate, and 34,317 severe/critical (SC) cases, as shown in [Table 1](#).
- Patients in the Severe/Critical category had significantly higher ECI and comorbidities compared to patients in the mild and moderate categories. Key comorbidities affecting more than 10% patients are shown in [Table 2](#).

Table 1. Baseline demographic characteristics of patients with COVID-19, stratified by severity of disease. (SD: Standard deviation – ICU: Intensive care unit)

Patient Characteristic	Severity of Disease at Index		
	Mild	Moderate	SC
N	160,326	189,240	34,317
Age - Mean (SD)	37.71 (17.1)	42.70 (16.5)	55.58 (14.9)
Gender: Female – n (%)	88,257 (55.0)	107,260 (56.7)	15,234 (44.4)
Payer: Medicare – n (%)*	4,106 (2.6)	9,027 (4.8)	6,812 (19.9)
Inpatient admission**	1,719 (1.1)	12,953 (6.8)	33,052 (96.3)
ICU Admission	N/A	N/A	11,932 (34.8)
Mechanical Ventilator Use	N/A	N/A	1,889 (5.5)
ECI – Mean (SD)	0.68 (1.15)	1.04 (1.49)	2.16 (2.35)
Elixhauser Category	0.68 (1.15)	1.04 (1.49)	2.16 (2.35)
0	100,972 (63.0)	97,347 (51.4)	10,506 (30.6)
1-2	47,196 (29.4)	65,356 (34.5)	12,034 (35.1)
3-4	9,935 (6.2)	20,019 (10.6)	6,979 (20.3)
5 or More	2,223 (1.4)	6,518 (3.4)	4,798 (14.0)

*All non-Medicare patients had commercial insurance.
**At any time during the duration of the disease.

Table 2. Baseline comorbidities of patients with COVID-19, stratified by severity of disease

	Severity of Disease at Index		
Comorbidities, n (%)	Mild	Moderate	SC
Cardiac Arrhythmia	4,359 (2.7)	9,398 (5.0)	3,933 (11.5)
Hypertension Uncomplicated	24,786 (15.5)	43,243 (22.9)	15,655 (45.6)
Chronic pulmonary disease	7,476 (4.7)	15,272 (8.1)	4,655 (13.6)
Diabetes Uncomplicated	8,592 (5.4)	16,210 (8.6)	7,631 (22.2)
Diabetes Complicated	5,787 (3.6)	11,230 (5.9)	6,487 (18.9)
Hypothyroidism	8,806 (5.5)	14,102 (7.5)	3,665 (10.7)
Renal failure	1,589 (1.0)	3,369 (1.8)	3,479 (10.1)
Obesity	12,785 (8.0)	21,546 (11.4)	6,484 (18.9)
Depression	13,417 (8.4)	20,197 (10.7)	3,959 (11.5)

References:

- NIH COVID-19 Treatment Guidelines. Available from: <https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/>.
- J&J. A Randomized, Double-blind, Placebo-controlled Phase 3 Study to Assess the Efficacy and Safety of Ad26.COV2.5 for the Prevention of SARS-CoV-2-mediated COVID-19 in Adults Aged 18 Years and Older - ENSEMBLE. November 6, 2020; Available from: <https://www.jnj.com/coronavirus/covid-19-phase-3-study-clinical-protocol>.
- <https://www.england.nhs.uk/coronavirus/post-covid-syndrome-long-covid/> - Accessed 4/21/2022

Abbreviations:

COVID-19: Coronavirus disease 2019
ECI: Elixhauser Comorbidity Index
GLM: Generalized linear model
ICU: Intensive Care Unit

CSS: COVID-19 signs and symptoms
OCS: Ongoing COVID-19 Symptoms
PCS: Post-COVID-19 Syndrome
SC: Severe/Critical
SD: Standard deviation

Key Findings

- Patients with COVID-19 in large claims databases were stratified by severity, using COVID-19 signs and symptoms and definitions of disease severity from the Janssen Phase 3 ENSEMBLE trial.
- Duration of disease was shown to increase from an average 19 days, to 28 and 61 days, for patients with mild, moderate and severe disease.
- Risk of Post-COVID-19 Syndrome increased from < 1% in mild cases to 20% in patients with severe disease.

Conclusions

- Nearly 20% patients with severe COVID-19 experienced Post-COVID-19 Syndrome.
- Severe COVID-19 at time of acute infection is the main predictor for Post-COVID-19 Syndrome.

- The mean (median, SD) duration of disease in the mild, moderate and severe cohorts was as follows: 18.8 (14, 15.3) days, 27.94 (15, 30.80) days, and 60.7 (36, 67.0) days, as shown in [Figure 1](#). Rates of OSC and PCS, by severity, are shown in [Figure 2](#).
- Severity at time of acute disease was the most significant risk factor for PCS [odds ratio (OR) for PCS in severe vs mild population (OR): 3.113 (95% confidence interval (CI): 2.336 - 4.149), OR for PCS in moderate vs mild population: 1.911 (95%CI: 1.838 - 1.988)]. Females (vs males) were also at increased odds of PCS (OR: 1.763 (95%CI: 1.667 - 1.864)). The odds for PCS also increased with age (independently of severity - in 10-year increment: OR for PCS: 1.746 (95%CI: 1.466 - 2.079). From all the COVID-19 signs and symptoms, somnolence and thrombosis at acute disease had the greatest association with PCS (OR: 1.911 (95%CI: 1.838 - 1.988) and OR: 1.787 (95%CI: 1.717 - 1.860), respectively).

Figure 1. Duration of Disease by COVID-19 severity (numbers represent mean duration).

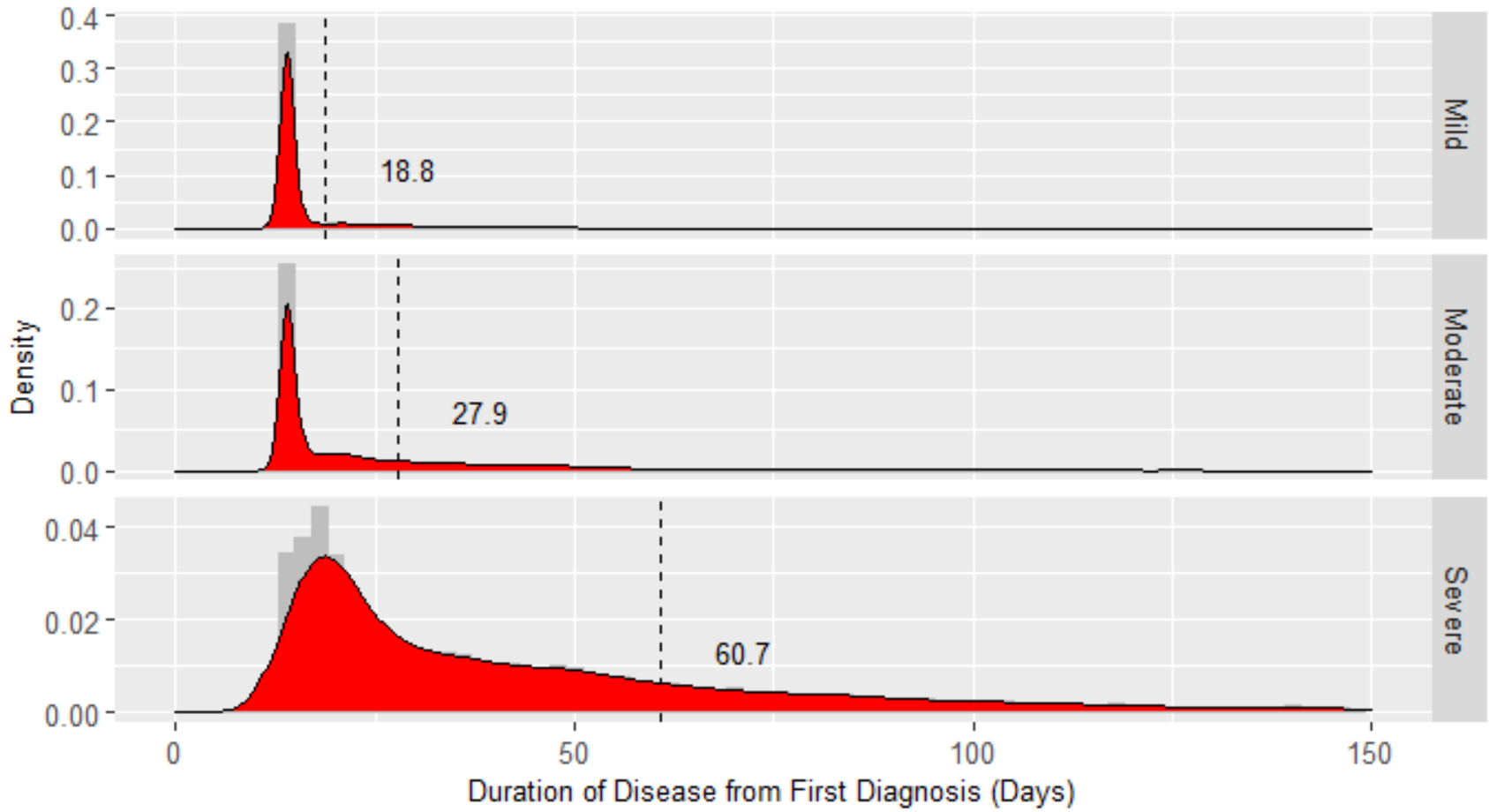


Figure 2. Percentage of patients with ongoing COVID-19 symptoms (OCS – characterized by a disease duration of 4-12 weeks) and Post-COVID-19 Syndrome (PCS – characterized by a disease duration > 12 weeks), by severity of disease.

