

## **Supplemental Section for**

### **Methylprednisolone and 60 Day Mortality in Hospitalized COVID-19 Pneumonia**

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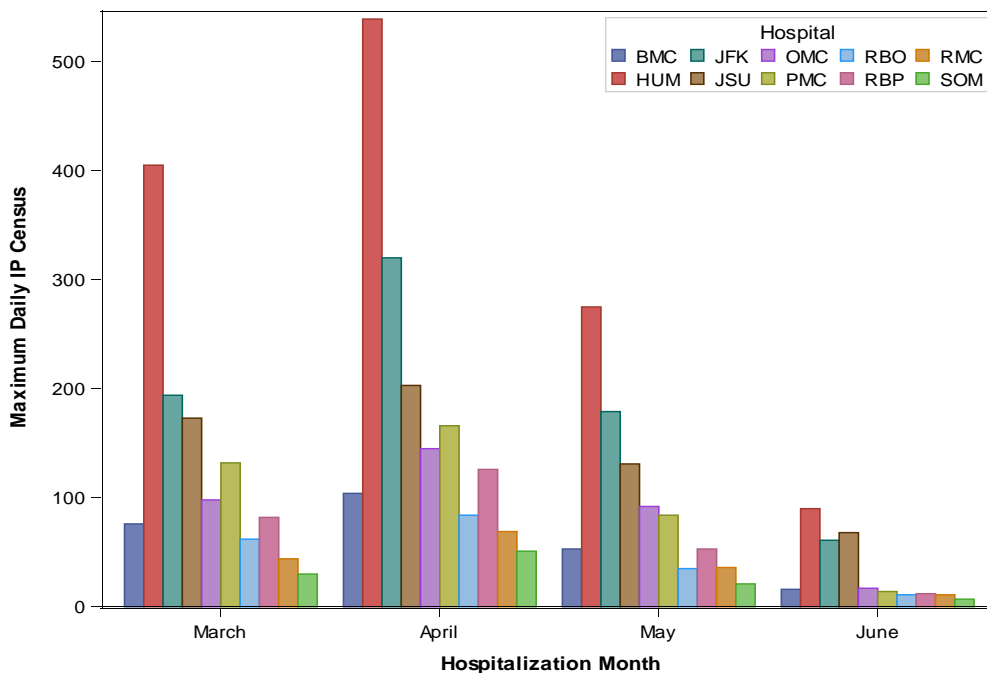
**Table S1.** Baseline Demographics Disease Characteristics on Unmatched Population and Propensity Score Matched Population.

Variable	Unmatched No methylprednisolone (N=645)	Unmatched Methylprednisolone (N=476)	P Value	Propensity score matched No methylprednisolone (N = 380)	Propensity Score matched Methylprednisolone (N = 379)	P Value
Age in years	64.00(53.00,79.00)	64.00(56.00,73.00)	0.6620	65.00(54.00,80.00)	64.00(55.00,74.00)	0.1129
Male	411(63.43)	219(53.03)	0.6079	238(62.14)	244 (64.21)	0.5175
Weight (kg)	81.20(68.70,90.72)	83.90(71.10,99.80)	0.0040	81.67(70.30,95.85)	83.90(71.45,99.80)	0.4270
BMI (kg/m <sup>2</sup> )	28.18(24.83,31.65)	29.48(25.94,34.30)	<.0001	29.82(25.51,32.80)	29.69(25.82,34.31)	0.1912
White	336(51.85)	154(23.77)	0.6079	198(51.70)	193(52.30)	0.5085
Asian	45(6.94)	31(7.51)	0.6079	20(5.22)	28(7.59)	0.5085
Black	91(14.04)	47(11.38)	0.6079	57(14.88)	42(11.38)	0.5085
Other	154(23.77)	229(54.01)	0.6079	94(24.54)	96(26.02)	0.5085
Community	527(81.33)	250(58.96)	<.0001	309(80.68)	220(7.89)	<.0001
Academic	121(18.67)	174(41.04)	<.0001	74(19.32)	160(42.11)	<.0001
Nursing Home	125(19.38)	43(10.26)	<.0001	308(80.42)	340(89.95)	<b>0.0002</b>
Former/Current smoker	116(19.86)	96(25.81)	0.0377	77(21.57)	88(25.81)	0.2334
Never smoker	468(80.14)	276(74.19)	0.0377	280(78.43)	253(74.19)	0.2334
SOB	412(63.78)	334(78.96)	<.0001	249(65.01)	298(78.63)	<.0001
Cough	417(64.75)	301(71.16)	0.0327	244(63.87)	271(71.32)	<b>0.0303</b>
AMS	109(17.33)	46(11.11)	0.0058	63(16.45)	41(10.79)	<b>0.0032</b>
GI	149(23.17)	88(20.90)	0.4077	76(19.90)	81(21.37)	0.6545
Anosmia or Ageusia	10(1.57)	9(2.20)	0.4834	6(1.58)	9(2.44)	0.4445
Duration of Symptoms prior to admission	5.00(2.00,7.00)	5.00(3.00,7.00)	0.0165	5.00(2.00,7.00)	5.00(3.00,7.00)	0.0523
Diabetes	214(33.18)	157(37.20)	0.1888	144(37.60)	139(36.58)	0.8221
COPD	27(4.19)	30(7.09)	0.0506	20(5.22)	28(7.37)	0.2360
Asthma	40(6.22)	40(9.48)	0.0569	24(6.27)	37(9.76)	0.0832
Cancer	61(9.46)	49(11.61)	0.2594	43(11.23)	43(11.32)	1.0000
CAD	86(13.33)	67(15.84)	0.2839	50(13.05)	61(16.05)	0.2594
CVA	28(4.35)	15(3.55)	0.6336	18(4.71)	14(3.68)	0.5887
CHF	51(7.96)	32(7.57)	0.9071	18(4.71)	28(7.37)	1.0000
Arrhythmia	65(10.12)	38(8.96)	0.5967	41(10.73)	30(7.89)	0.2126
Renal Failure	40(6.23)	33(7.78)	0.3249	28(7.31)	31(8.16)	0.6862
Rheumatologic Disease	15(2.33)	22(5.20)	0.0159	10(2.61)	19(5.01)	0.0909
qSOFA 0	375(59.62)	225(54.35)	0.2544	224(58.49)	222(58.42)	0.7647
qSOFA 1	199(31.64)	156(37.68)	0.2544	130(33.94)	130(34.21)	0.7647
qSOFA 2	51(8.11)	31(7.49)	0.2544	28(7.31)	26(6.84)	0.7647
qSOFA 3	4(0.64)	2(0.48)	0.2544	1(0.26)	2(0.53)	0.7647
O2 sat < 94%	305(48.41)	225(57.25)	0.0069	216(56.40)	218(57.37)	0.8265
Temperature	99.00(98.00,100.70)	99.30(98.00,100.80)	0.0476	98.80(97.70,100.40)	99.25(98.00,100.65)	<b>0.0027</b>
Heart Rate	95.00(82.00,108.00)	95.00(82.00,108.00)	0.0581	95.00(84.00,108.00)	97.00(86.00,108.00)	0.2467
Respiratory Rate	19.00(18.00,21.00)	20.00(18.00,22.00)	0.0097	19.00(18.00,22.00)	20.00(18.00,22.00)	0.2622
Nasal Cannula	227(82.85)	137(66.50)	0.0005	161(82.14)	132(66.00)	<b>0.0045</b>
Venti mask	4(1.46)	3(1.46)	0.0005	2(1.02)	3(1.50)	<b>0.0045</b>
High Flow	8(2.92)	15(7.28)	0.0005	6(3.06)	15(7.50)	<b>0.0045</b>
CPAP	1(0.36)	2(0.97)	0.0005	1(0.51)	2(1.00)	<b>0.0045</b>
BPAP	0(0.00)	2(0.97)	0.0005	0(0.00)	2(1.00)	<b>0.0045</b>
Mechanical Ventilation	55(10.62)	138(39.88)	<.0001	35(11.08)	129(39.09)	<.0001
WBC	6.50(5.00,9.10)	6.50(5.10,9.50)	0.5947	6.60(5.10,9.20)	6.50(5.10,9.55)	0.8365
HGB	13.40(12.00,14.50)	13.50(12.20,14.80)	0.2190	13.40(12.20,14.50)	13.50(12.20,14.70)	0.5022
PLT	200.00(158.00,251.00)	186.00(147.00,251.00)	0.0596	203.00(161.00,259.00)	189.50(147.00,252.00)	<b>0.0238</b>

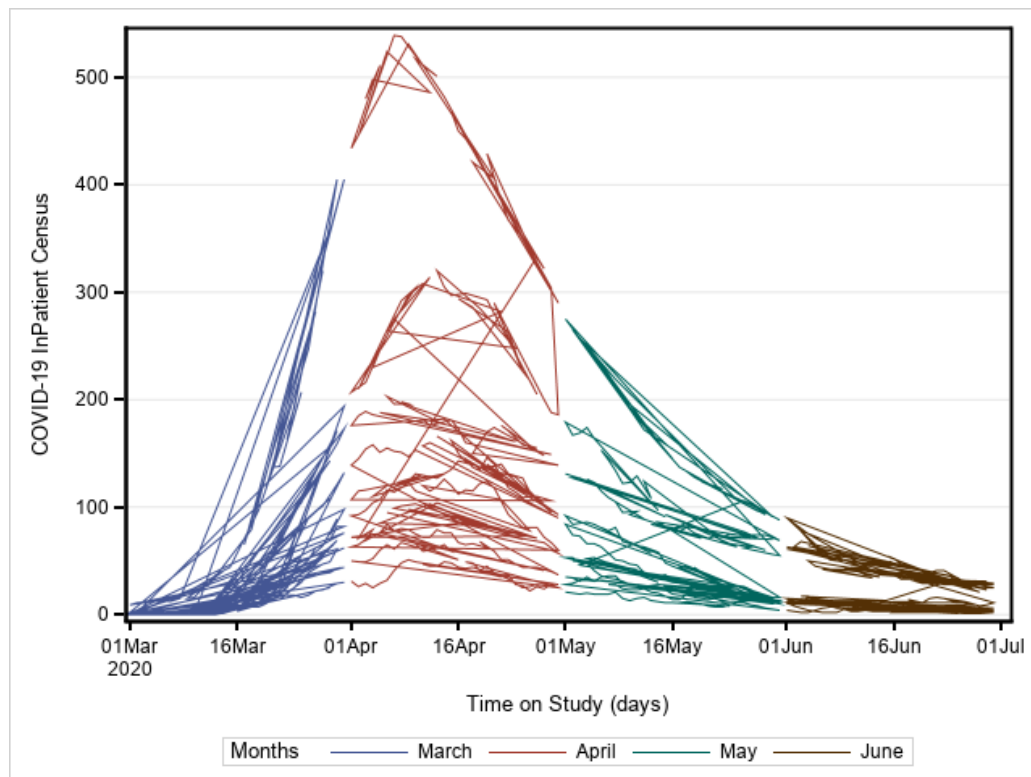
ALC	0.90(0.60,1.20)	0.79(0.60,1.10)	0.0007	0.90(0.60,1.30)	0.80(0.60,1.10)	<b>0.0004</b>
IL6	11.50(5.00,34.00)	12.00(5.00,32.00)	0.6607	12.50(5.00,37.50)	12.00(5.00,31.50)	0.8044
CRP	10.91(5.20,20.79)	13.11(7.09,20.20)	0.0444	11.71(5.34,22.10)	13.40(7.10,20.34)	0.3187
D-Dimer	1.01(0.64,2.11)	0.98(0.61,1.89)	0.7909	1.01(0.65,2.07)	0.98(0.61,1.91)	0.8118
Ferritin	641.89(320.65,1453.60)	838.96(430.40,1569.80)	0.0044	727.45(331.61,1470.50)	853.21(444.90,1569.80)	<b>0.0231</b>
Creatinine	1.00(0.80,1.40)	1.01(0.80,1.33)	0.9379	1.01(0.80,1.49)	1.01(0.80,1.35)	0.2327
Troponin	0.03(0.01,0.30)	0.02(0.01,0.09)	0.0516	0.03(0.01,0.30)	0.02(0.01,0.09)	0.1355
BNP	103.70(29.85,701.30)	88.80(26.20,362.00)	0.1702	129.70(40.60,941.10)	85.25(25.60,339.35)	<b>0.0141</b>
Hydroxychloroquine	463(73.73)	333(88.33)	<.0001	270(71.81)	318(88.58)	<b>&lt;.0001</b>
Azithromycin	438(70.19)	277(73.47)	0.2793	256(68.45)	264(73.33)	0.1672
Remdesivir	4(0.65)	63(16.80)	0.0061	3(0.81)	10(2.81)	0.0512
Tocilizumab	31(5.01)	11(2.94)	<.0001	14(3.78)	64(17.88)	<b>&lt;.0001</b>
Convalescent Plasma	0(0.00)	4(28.57)	0.0002	0(0.00)	4(28.57)	<b>0.0015</b>
ECMO	1(0.17)	9(2.43)	0.0011	1(0.28)	9(2.54)	<b>0.0104</b>
Dialysis	19(3.09)	11(2.92)	0.8748	14(3.78)	11(3.04)	0.6853

HR = Hazard Ratio; CI = Confidence Interval; SOB = Shortness of Breath; AMS = Altered Mental Status; GI = Gastrointestinal Symptoms; PTA = Prior to admission; COPD = Chronic Obstructive Disease; CAD = Coronary Artery Disease; CVA = Cerebrovascular Accident; CHF = Congestive Heart Failure; LFTs = elevated liver function tests; qSOFA = Quick Sepsis Related Organ Failure Assessment; HCQ = Hydroxychloroquine; AZ = Azithromycin; MP = Methylprednisolone; HD MP = High Dose Methylprednisolone; LD MP = Low Dose Methylprednisolone; WBC= White Blood Cells; HGB = Hemoglobin; PLT = Platelet; ALC = Absolute Lymphocyte Count; ECMO = Extracorporeal Membrane Oxygenation

**Figure S1.** Bar plot of COVID-19 Hospitalizations in the 13 HMH Hospitals from March – June 2020. Hackensack University Medical Center (HUM) has 4 hospitals combined.



**Figure S2.** Spaghetti plot of inpatient COVID-19 patients in 13 HMH Hospitals between March to June 2020.



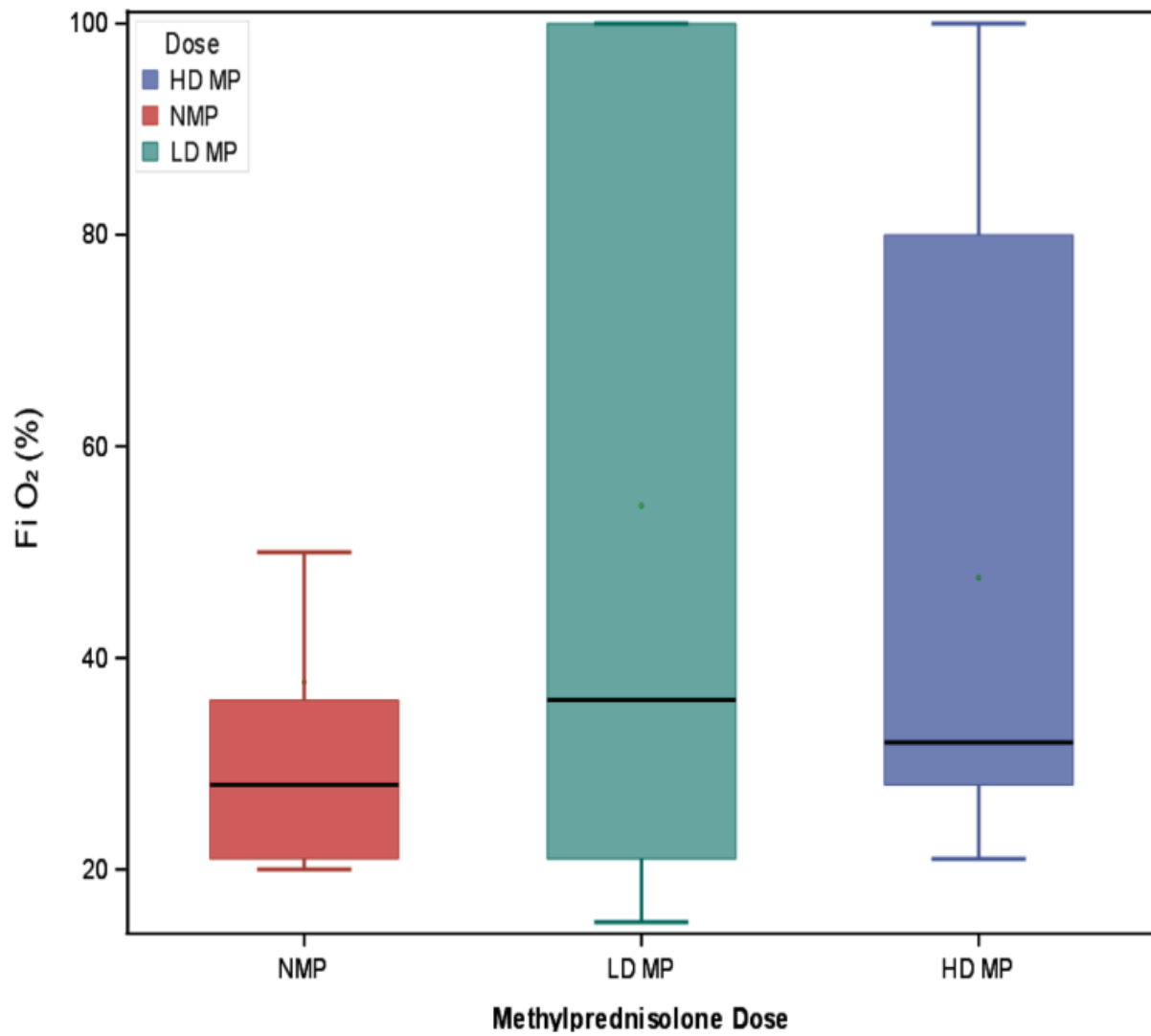
**Table S2.** Univariate and Multivariate Cox Regression Analyses of Propensity Score Matched Population

Univariate Cox Regression			Multivariate Cox Regression		
Comparison	HR (95% CI)	P-Value	Comparison	HR (95% CI)	P-Value
Male vs Female	1.20 (0.93, 1.56)	0.1691	<b>Model 1: MP vs NMP</b>		
Age>60 vs <60	2.83 (2.05, 3.91)	<.0001	MP vs NMP	0.40(0.27,0.59)	<0.0001
Current vs Non Smoker	0.62(0.29, 1.32)	0.2154	Nursing home vs Residential	3.08(1.94,4.89)	>0.0001
Former vs Current Smoker	1.21(0.91, 1.61)	0.1934	CAD vs None	2.12(1.38,3.27)	0.0006
Unknown Race vs Asian	2.08(1.11, 3.89)	0.0224	Invasive Mechanical Ventilation vs None	2.87(1.64,5.02)	0.0002
Black vs Asian	1.00(0.56, 1.79)	0.9926	Non-Mechanical Ventilation Oxygen Support vs None	1.11(0.60,2.05)	0.7483
Other Race vs Asian	1.12(0.65, 1.91)	0.6887	<b>Model 2: Dose (LD or HD) vs NMP</b>		
White vs Asian	1.33(0.81, 2.20)	0.2651	HD MP vs NMP	0.48(0.30,0.77)	0.0025
Academic vs Community Hospital	1.18 (0.91, 1.52)	0.2105	LD MP vs NMP	0.35(0.22,0.53)	<0.0001
Nursing Home vs Home	2.81(1.99, 3.96)	<.0001	Nursing Home vs Residential	2.95(1.83,4.76)	<0.0001
<b>Symptoms</b>			CAD vs None	2.22 (1.44,3.42)	0.0003
Fever vs None	0.88 (0.67, 1.15)	0.3445	Invasive Mechanical Ventilation vs None	2.77(1.58,4.86)	0.0004
SOB vs None	1.18 (0.91, 1.53)	0.2233	Non-Mechanical Ventilation Oxygen Support vs None	1.13(0.61,2.09)	0.6992
Cough vs None	0.79 (0.61, 1.01)	0.0641	<b>Model 3: Dose and Duration</b>		
AMS vs None	3.14(2.32, 4.26)	<.0001	HD MP 7-14 Days vs LD MP 7-14 days	1.91(0.82,4.45)	0.1338
GI vs None	0.66(0.47, 0.93)	0.0185	HD MP ≥14 days vs LD MP ≥ 14 days	1.07(0.44,2.59)	0.8899
Anosmia or Ageusia vs None	NA	<.0001	HD MP ≤ 7 days vs LD MP ≤ 7 days	1.36 (0.78,2.38)	0.2836
Duration of Symptoms PTA > 7 vs ≤ 7 days	0.61 (0.41, 0.91)	0.0143	LD MP 7-14 days vs LD MP ≥ 14 days	1.27(0.60,2.69)	0.5434
<b>Comorbidities</b>			LD MP 7-14 days vs LD MP ≤ 7 days	0.45(0.22,0.91)	0.0273
Diabetes vs None	1.06 (0.82, 1.37)	0.6503	LD MP ≥ 14 days vs NMP	0.16(0.09,0.28)	<0.0001
COPD vs None	2.44 (1.64, 3.63)	<.0001	LD MP ≤ 7 days vs NMP	0.46 (0.29,0.73)	0.001
Asthma vs None	0.89 (0.56,1.41)	0.6042	<b>Model 4: Methylprednisolone vs Tocilizumab</b>		
COPD/Asthma vs None	1.49(1.07, 2.05)	0.0169	MP vs TOC	0.32 (0.12,0.86)	0.0231
Hypertension vs None	2.12 (1.60, 2.81)	<.0001	MP and TOC vs TOC	0.26 (0.09,0.73)	0.0116
Cancer vs None	2.08 (1.46, 2.97)	<.0001	<b>Model 5: MP Dose (LD or HD) vs Tocilizumab</b>		
CAD vs None	2.09 (1.56, 2.79)	<.0001	HD MP and TOC vs TOC	0.26 (0.08,0.86)	0.0260
CVA vs None	2.24 (1.44, 3.50)	0.0004	LD MP vs TOC	0.26 (0.09, 0.73)	0.0116
CHF vs None	2.12 (1.41, 3.21)	0.0004	LD MP and TOC vs TOC	0.26 (0.09, 0.74)	0.0122
Arrhythmia vs None	2.07 (1.43, 2.98)	0.0001			
Renal Failure vs None	1.95 (1.37, 2.78)	0.0002			
Dialysis vs None	0.74 (0.39, 1.43)	0.3726			
Elevated LFTS vs None	1.03 (0.80, 1.33)	0.8142			
<b>Oxygen Support</b>					
Low Oxygen Saturation vs None	0.99 (0.77, 1.28)	0.9307			
Invasive Mechanical Ventilation vs None	1.62 (1.16, 2.27)	0.0051			
Non-Mechanical Ventilation Oxygen Support Vs None	0.98 (0.64, 1.50)	0.9233			
<b>qSOFA</b>					
qSOFA 3 vs 0	10.23 (5.00, 20.96)	<.0001			
qSOFA 2 vs 0	3.64 (2.41, 5.50)	<.0001			
qSOFA 1 vs 0	1.42 (1.07, 1.90)	0.0169			
<b>COVID-19 Treatment</b>					
Hydroxychloroquine vs None	0.41 (0.30, 0.56)	<.0001			
Azithromycin vs None	0.64 (0.49, 0.84)	0.0012			

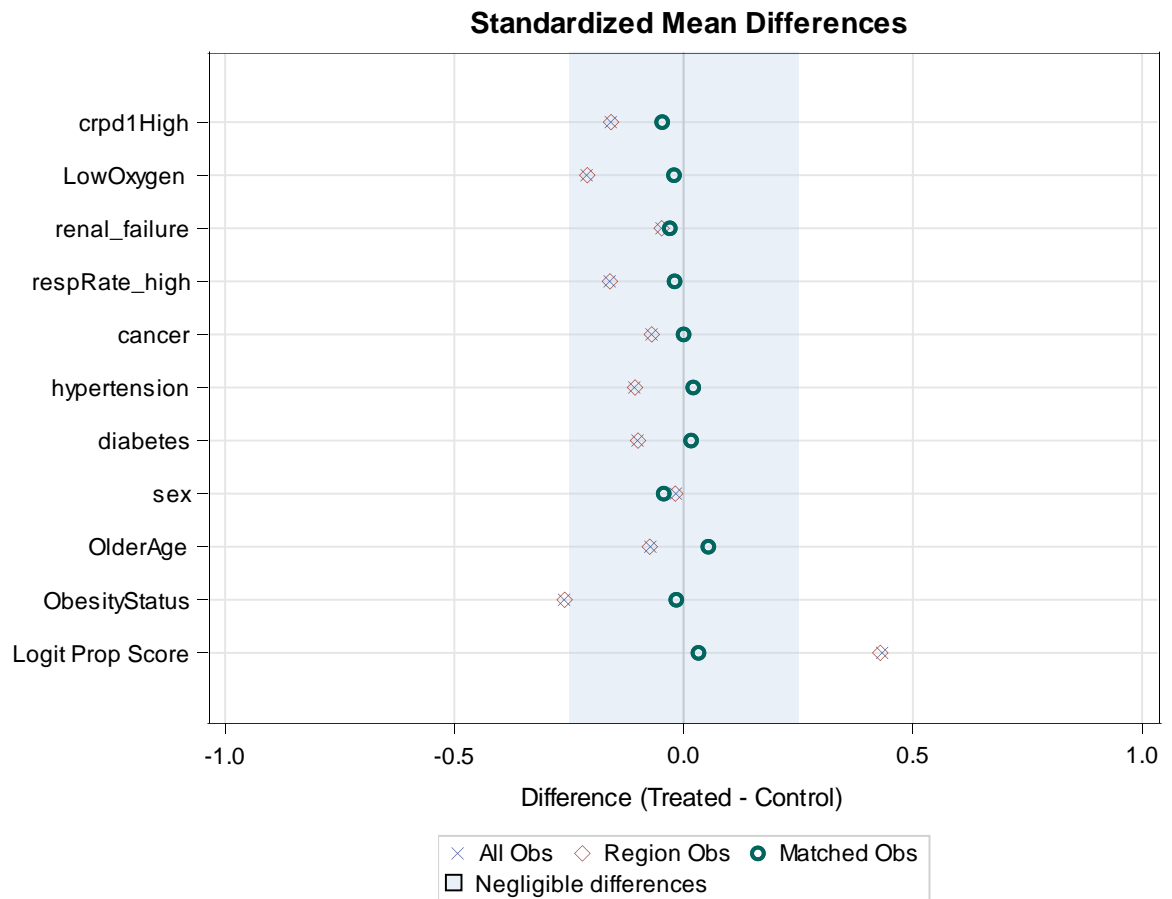


HCQ and Az vs None	0.89 (0.19, 4.26)	0.8860		
Remdesivir vs None	0.78 (0.34, 1.81)	0.5637		
Tocilizumab vs None	0.68 (0.47, 0.98)	0.0407		
Convalescent Plasma vs None	0.23 (0.03, 1.74)	0.1558		
<b><i>Methylprednisolone</i></b>				
<b><i>Dose</i></b>				
MP vs NMP	0.44 (0.33, 0.60)	<.0001		
HD MP vs NMP	0.61 (0.44, 0.85)	0.0033		
LD MP vs NMP	0.34 (0.24, 0.48)	<.0001		
<b><i>Duration</i></b>				
MP $\leq 7$ vs $> 7$ days	1.86 (1.36, 2.56)	<.0001		
HD MP $\leq 7$ vs $> 7$ days	2.00 (1.25, 3.20)	0.0039		
HD vs LD MP $\leq 7$ days	1.73 (1.11, 2.70)	0.0157		
HD MP $\leq 7$ days vs LD MP $> 7$ days	4.01 (2.45, 6.57)	<.0001		
HD MP $\leq 7$ days vs NMP	0.82 (0.55, 1.20)	0.3095		
HD MP $> 7$ days vs LD MP $\leq 7$ days	0.87 (0.55, 1.35)	0.5364		
HD MP $> 7$ days vs LD MP $> 7$ days	2.01 (1.22, 3.30)	0.0061		
HD MP $> 7$ days vs NMP	0.41 (0.26, 0.62)	<.0001		
LD MP $\leq 7$ vs $> 7$ days	2.32 (1.43, 3.75)	0.0006		
LD MP $\leq 7$ days vs NMP	0.47 (0.32, 0.71)	0.0002		
LD MP $> 7$ days vs NMP	0.20 (0.13, 0.32)	<.0001		
<b><i>Timing from Onset of Symptoms</i></b>				
$>7-14$ days vs $\leq 7$ days	0.70 (0.49, 0.99)	0.0462		
$>14$ days vs $\leq 7$ days	0.32 (0.16, 0.63)	0.0010		

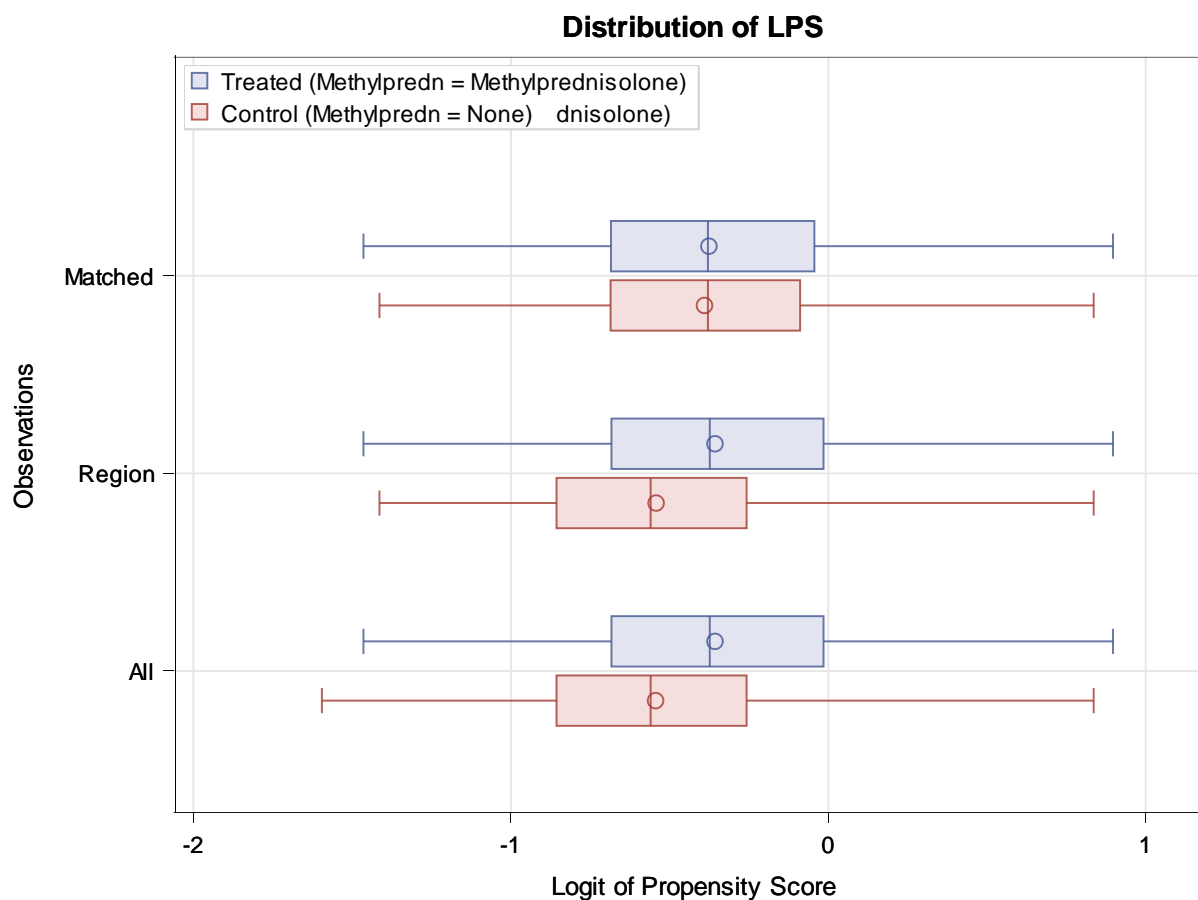
**Figure S3.** Boxplot of fraction of inspired oxygen ( $FiO_2$ ) reported on COVID-19 patients NMP, LD MP, and HD MP.



**Figure S4.** Plot of differences Methylprednisolone – No Methylprednisolone in hospitalized COVID-19 patients. The plot shows that the differences were very close to zero as were the Logit propensity scores.

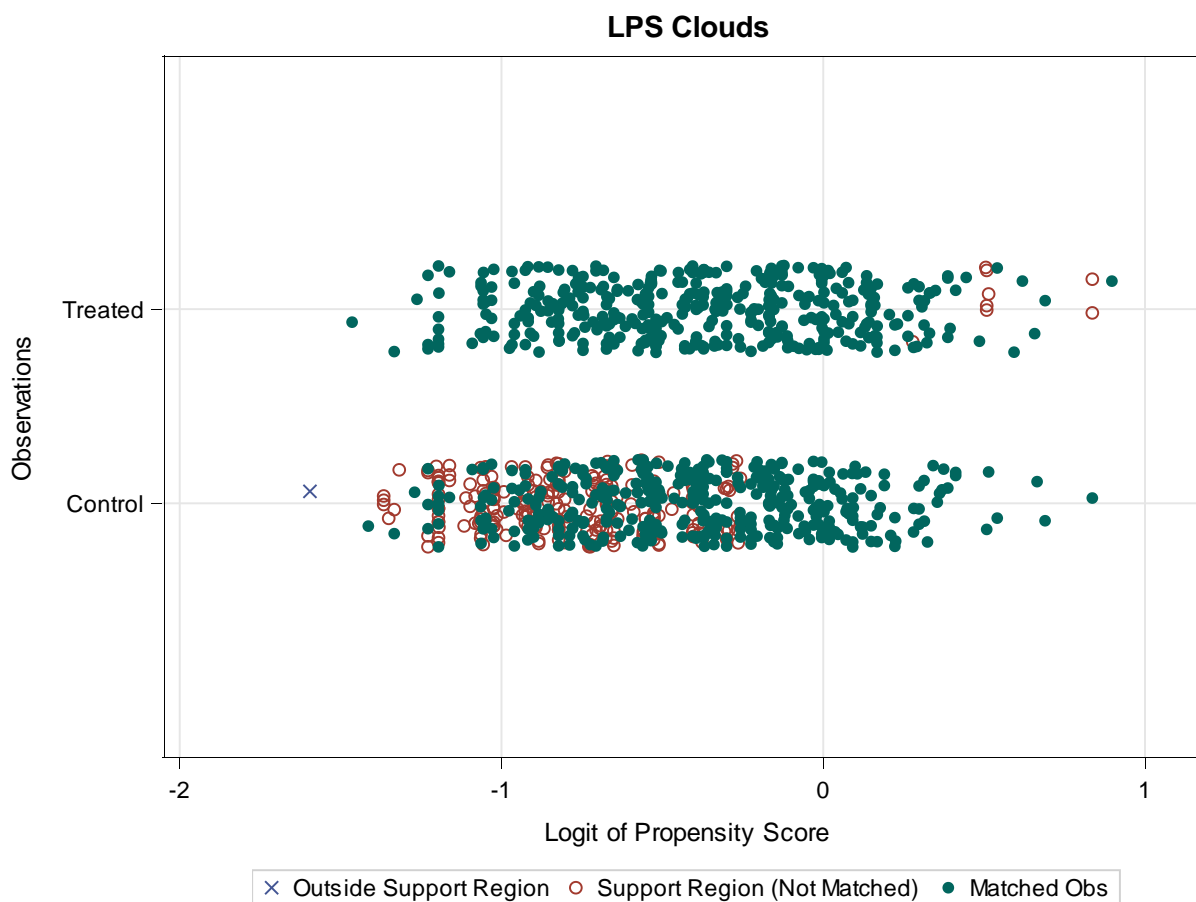


**Figure S5.** Comparison Boxplots of distributions of Logit of Propensity Scores for MP– NMP treated COVID-19 patients. The boxplots show that the two distributions are well balanced for the MP-NMP matched observations.

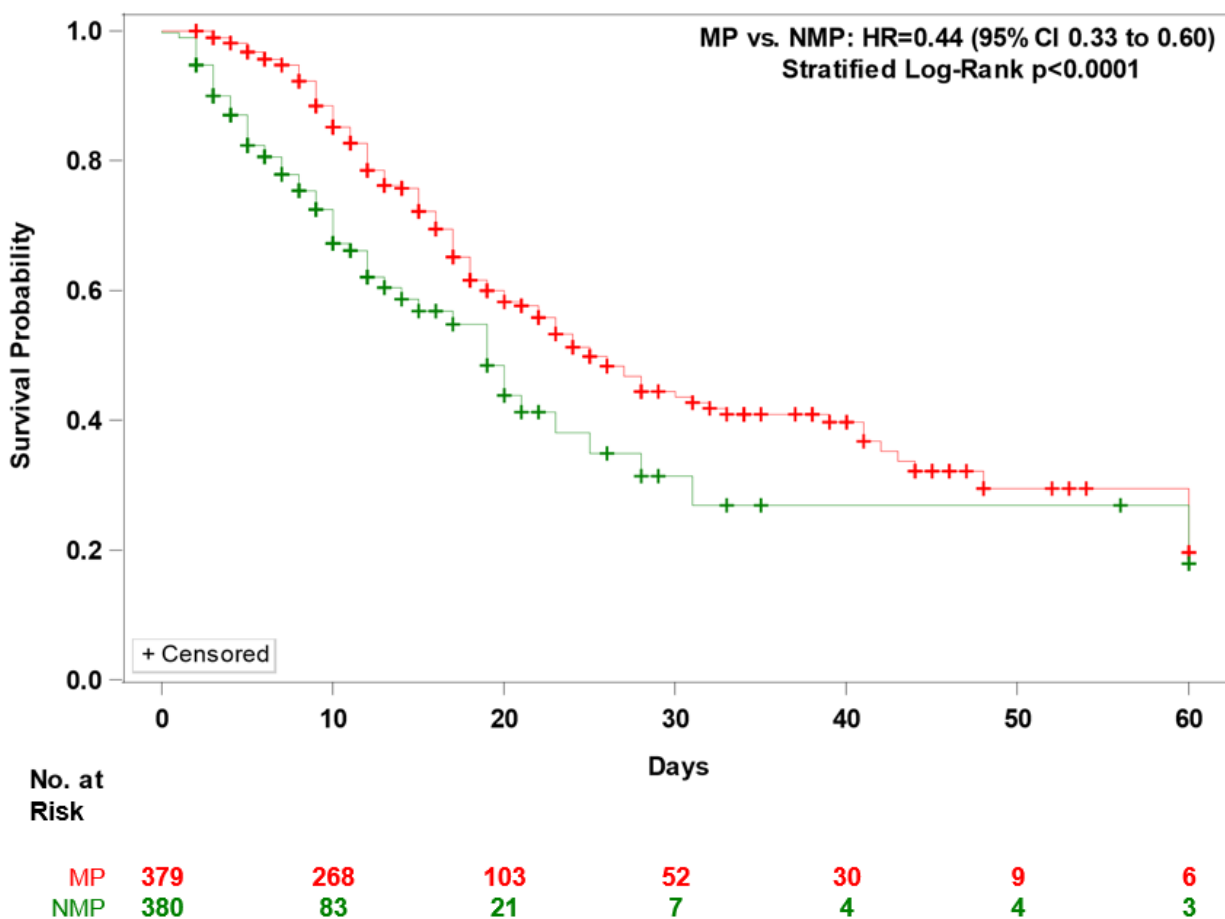


**Figure S6.** LPS Cloud Plots showing Distributions of Logit of Propensity Scores for MP and NMP treated COVID-19 patients. The propensity matching procedure failed to match only 8 of the methylprednisolone patients with any of patients who did not receive methylprednisolone during their COVID-19 hospitalization.

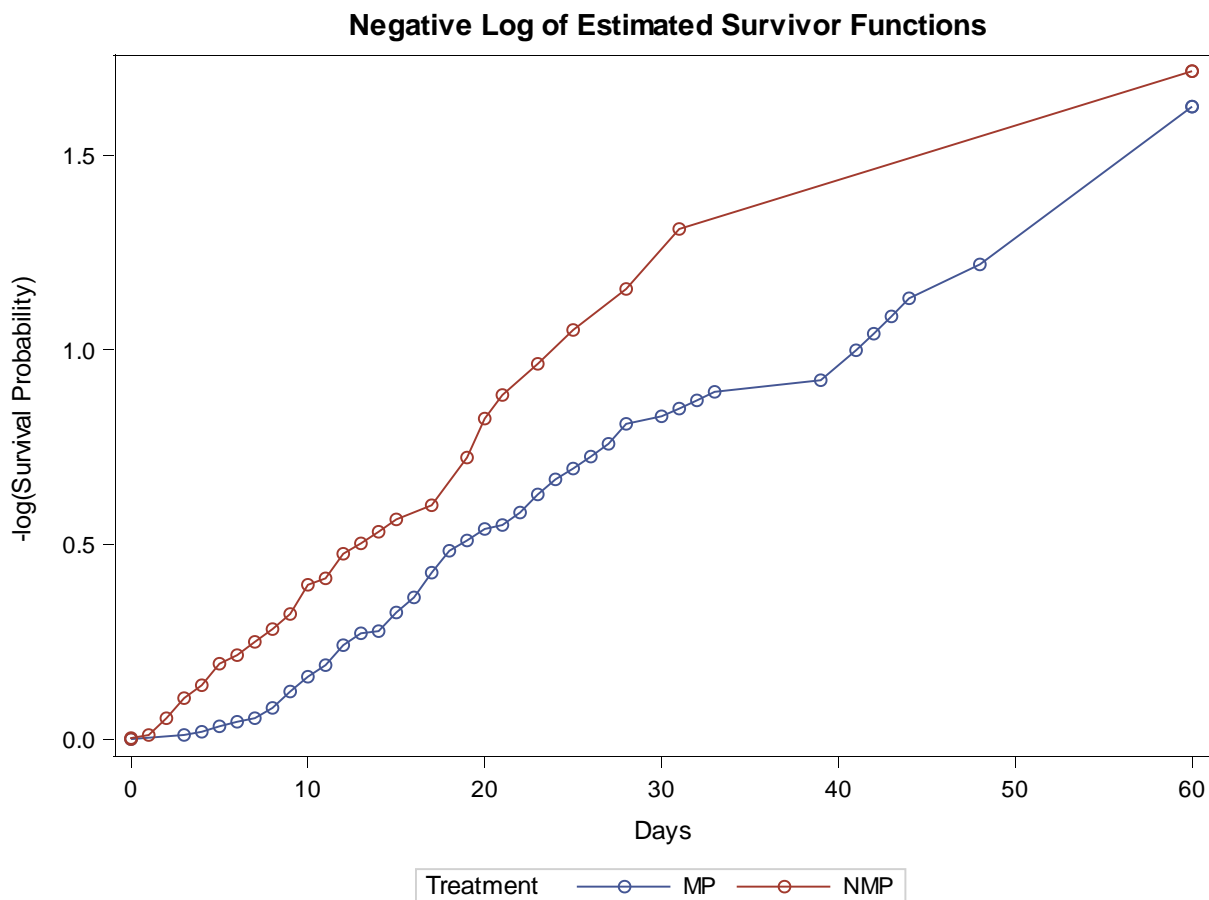
Taken together, Table S1 and Table S2 and Figures S1-S3 show that that propensity matched sample of 384 pairs yielded reasonably well-balanced distributions to conduct subsequent analyses.



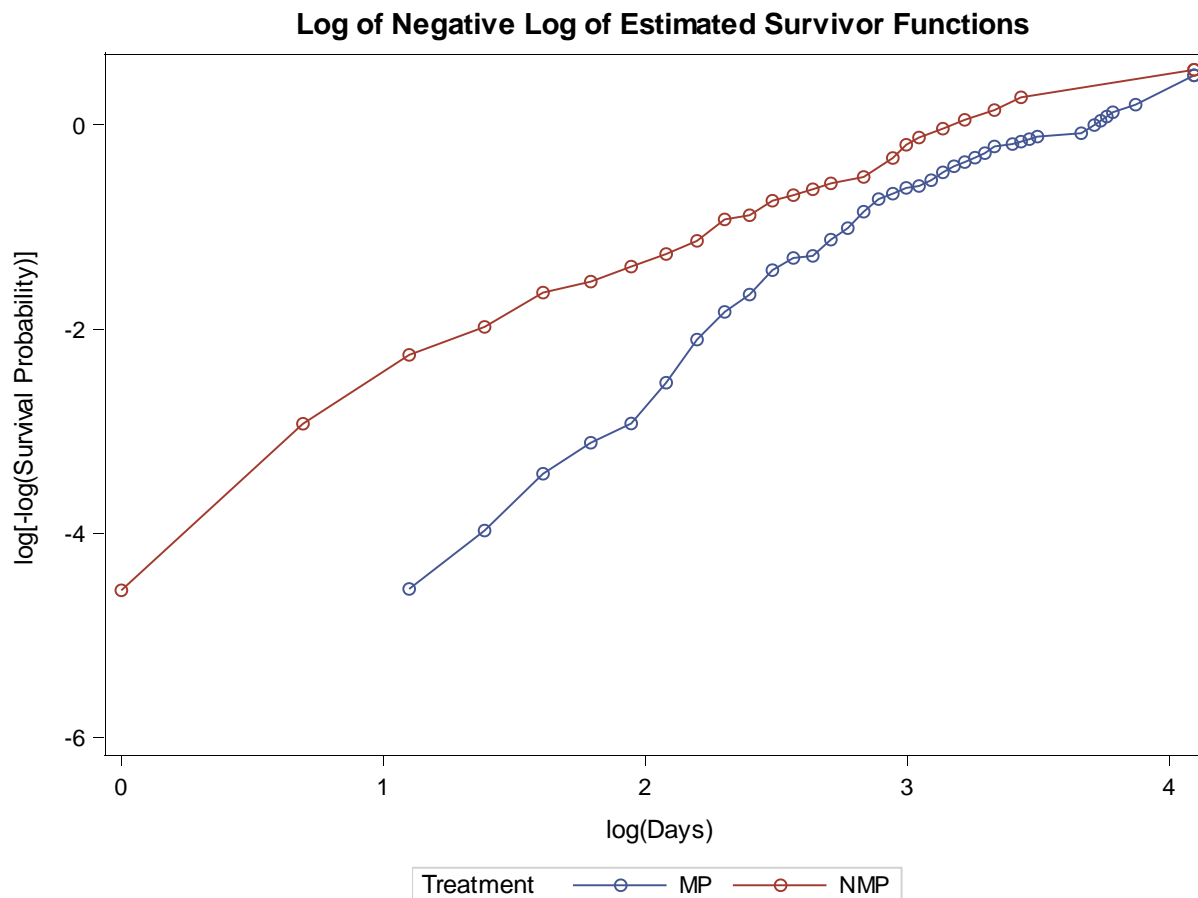
**Figure S7.** Kaplan-Meier Plot of in-hospital survival for no methylprednisolone (NMP) and methylprednisolone (MP) treated cohorts in admitted COVID-19 patients. Out of the 380 patients in the NMP cohort, 99 (25.8%) expired during COVID-19 hospital stay. Out of the 379 patients in the MP cohort, 143 (33.6%) expired during COVID-19 hospital stay. 30-Day and 60-Day in-hospital survival for the NMP cohort were 31.5% (95% CI 19.0% to 45.4%) and 18.0% (95% CI 4.5% to 37.7%), respectively. 30-Day and 60-Day In-hospital survival for the MP cohort were 43.6% (95% CI 36.5% to 50.9%) and 19.7% (95% CI 8.7% to 33.8%), respectively. The difference in In-hospital survival between the NMP (median=25.0 days (95% CI 22.0 to 32.0 days)] and MP (median =19.0 days (95% CI 14.0 to 25 days)] was statistically significant (Stratified Log-rank  $P < 0.0001$ ). These data indicate there was survival benefit for the patients that were treated with methylprednisolone.



**Figure S8.** A plot of log cumulative hazard function ( $-\log(\text{survival function})$ ) by time for MP and NMP treated COVID-19 patients. The plot showed that cumulative hazard function made a sharp increase by day 40 and the no methylprednisolone cohort had a mild slowing rate around 30 days. This graph indicates that the methylprednisolone the proportional hazard assumption may not been satisfied.

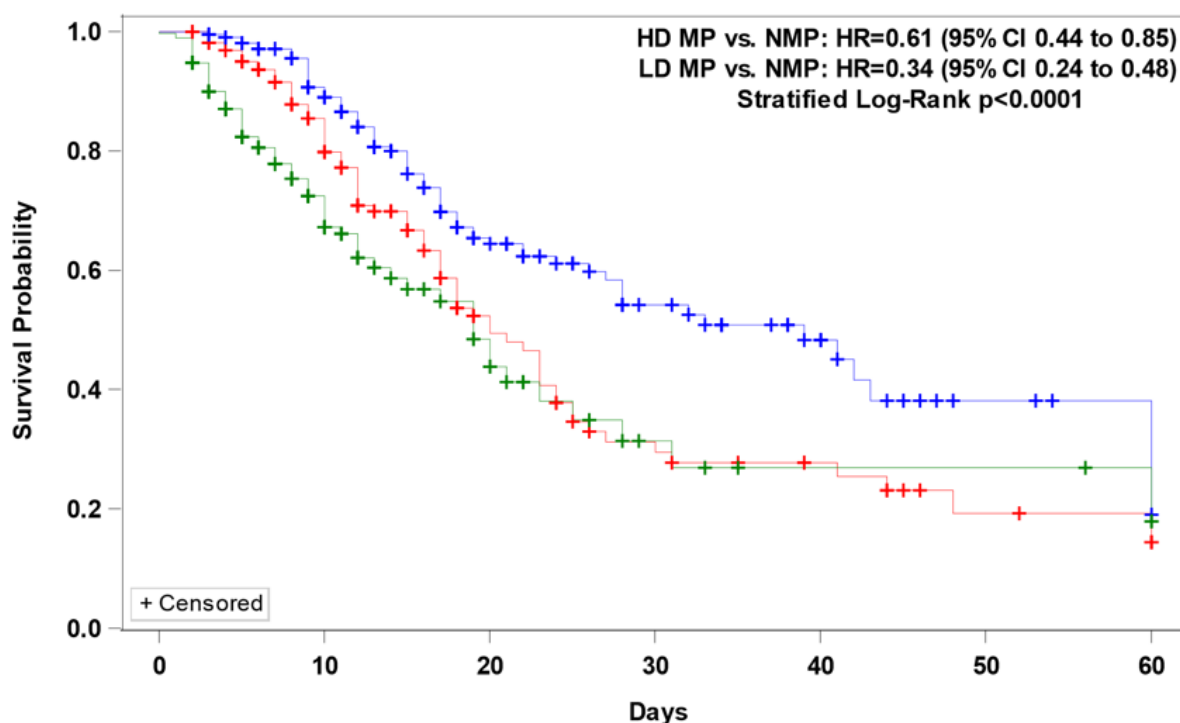


**Figure S9.** A plot of log cumulative hazard function ( $-\log(\text{survival function})$ ) by  $\log(\text{time})$  in MP and NMP treated COVID-19 patients. The shows that hazard in the methylprednisolone cohort were increasing more rapidly after 2 ( $\log(\text{Days})$ ) indicating there was a possible interaction between methylprednisolone and days since admission.



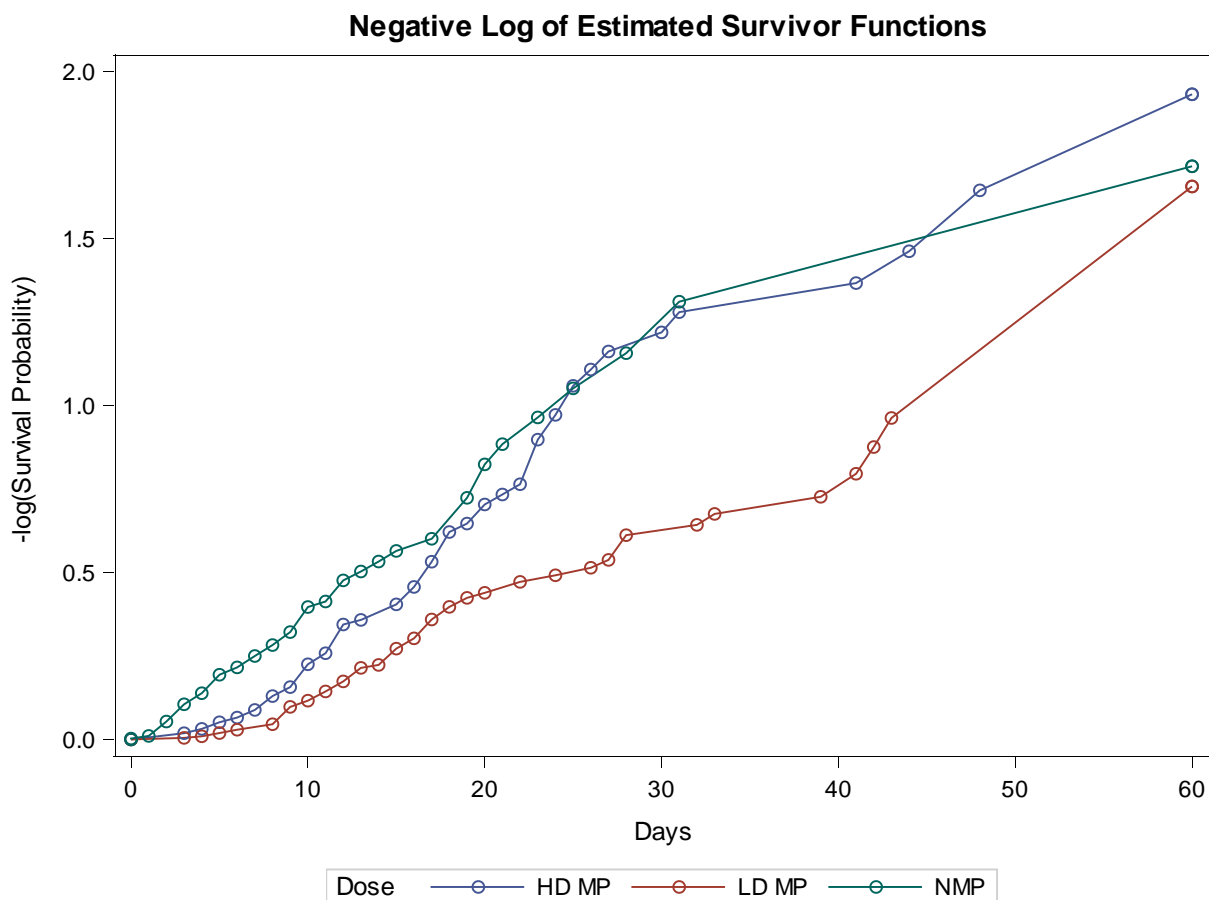


**Figure S10.** Kaplan-Meier Plot of in-hospital survival for no methylprednisolone (NMP), low dose methylprednisolone (LD MP) and high dose methylprednisolone (HD MP) treated cohorts in admitted COVID-19 patients. Out of the 380 patients in the NMP cohort, 99 (25.8%) expired during COVID-19 hospital stay. Out of the 215 patients in the LD MP cohort, 69 (31.9%) expired during COVID-19 hospital stay. Out of the 164 patients in the HD MP cohort, 74 (55.2%) expired during COVID-19 hospital stay. 30-Day and 60-Day in-hospital survival for the NMP cohort were 31.5% (95% CI 19.0% to 45.4%) and 18.0% (95% CI 4.5% to 37.7%), respectively. 30-Day and 60-Day In-hospital survival for the LD MP cohort were 54.2% (95% CI 44.8% to 63.5%) and 19.1% (95% CI 1.1% to 51.4%), respectively. 30-Day and 60-Day In-hospital survival for the HD MP cohort were 29.6% (95% CI 19.8% to 40.4%) and 14.4% (95% CI 5.0% to 27.9%), respectively. The difference in In-hospital survival between the NMP (median=25.0 days (95% CI 22.0 to 32.0 days)) and LD MP (median =39.0 days (95% CI 27.0 to N/A days)) and HD MP (median =20.0 days (95% CI 17.0 to 24 days)) was statistically significant (Stratified Log-rank  $P < 0.0001$ ). These data indicate there was survival benefit for the patients that were treated with LD MP throughout the Day 60 follow-up. In contrast, the HD MP had survival benefit over not the NMP but the KM plot show by Day 18 the benefit had diminished such that the HD MP and NMP were crisscrossing all the way through Day 40, beyond which in-hospital survival kept declining below the MP cohort.

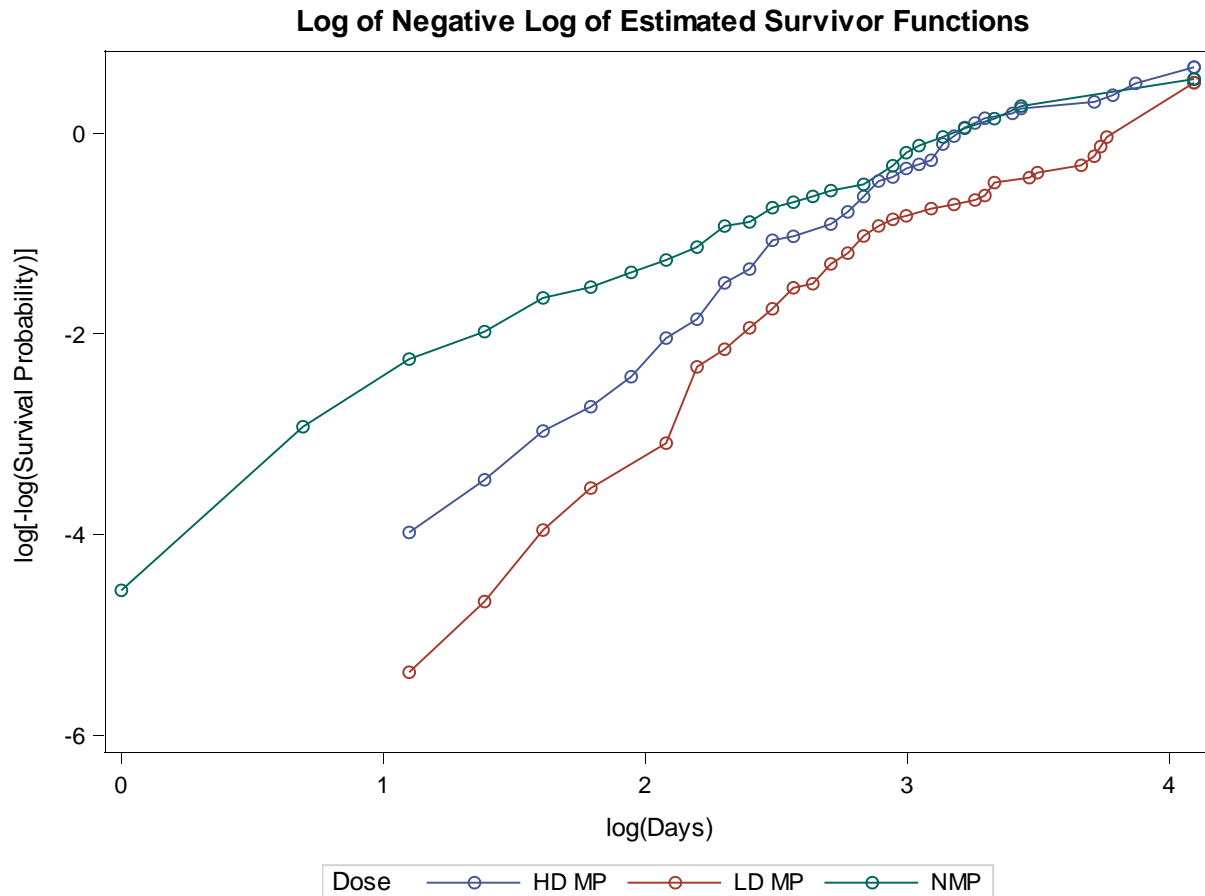


No. at Risk	0	10	20	30	40	50	60
HD MP	164	106	36	18	12	5	4
LD MP	215	162	67	34	18	4	2
NMP	380	83	21	7	4	4	3

**Figure S11.** The plot of  $\log(\text{cumulative hazard})$ (-negative survival) by days for the NMP, LD MP and HD MP treated COVID-19 patients. The graph shows that cumulative hazard in HD and LD methylprednisolone were increased and in particular the HD MP was increasing much faster than LD after 40 days, this suggests that the proportional hazard assumption may not have been met.

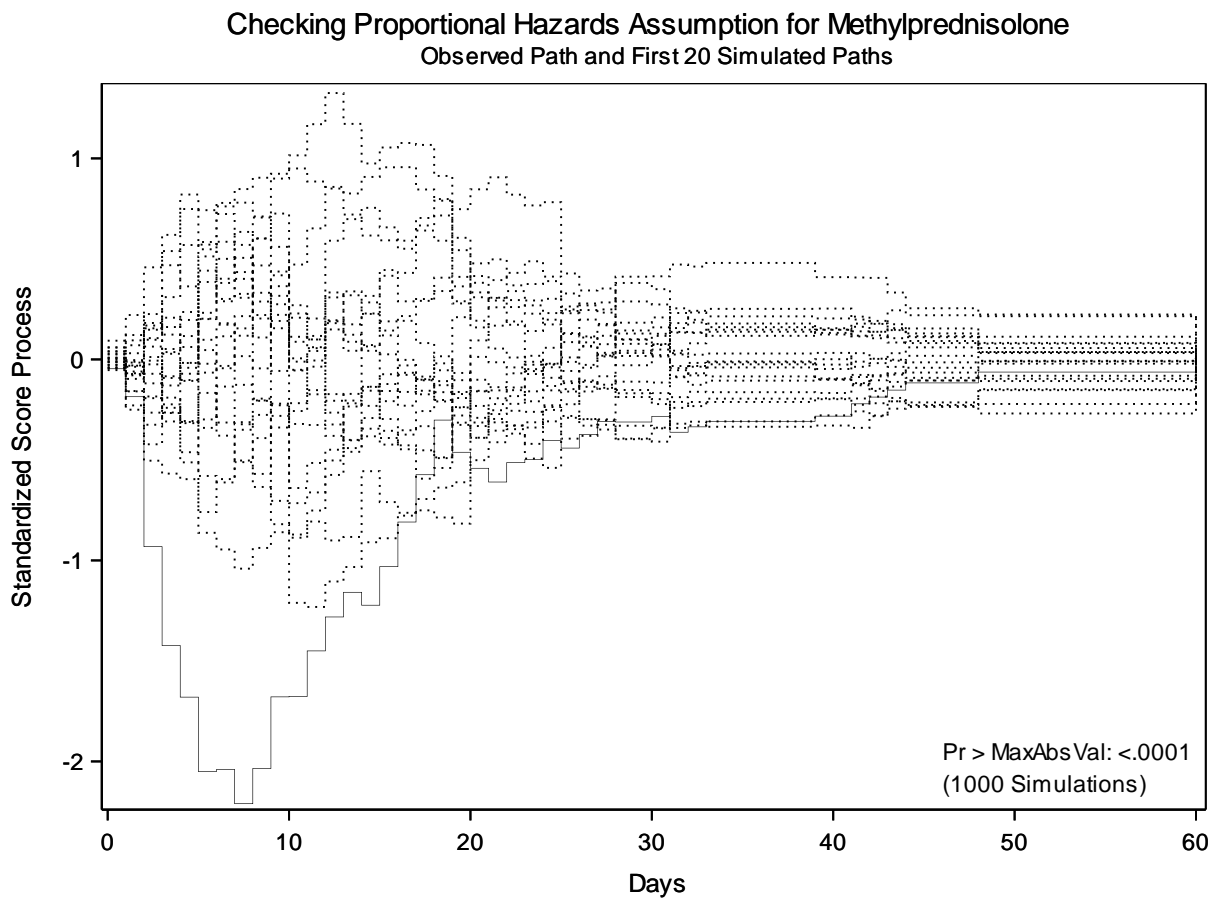


**Figure S12.** The plot of log cumulative hazard (-negative survival) by log (days) in NMP , LD MP , HD MP treated COVID-19 patients. show that cumulative hazard in HD and LD methylprednisolone were increase and in particular the HD MP was increasing much faster than LD after 2 log days, and by 3 log days, the HD MP and NMP are the same path while LD increased slowly before increasing faster before 4 log days. This suggest that the proportional hazard assumption may not have been met.

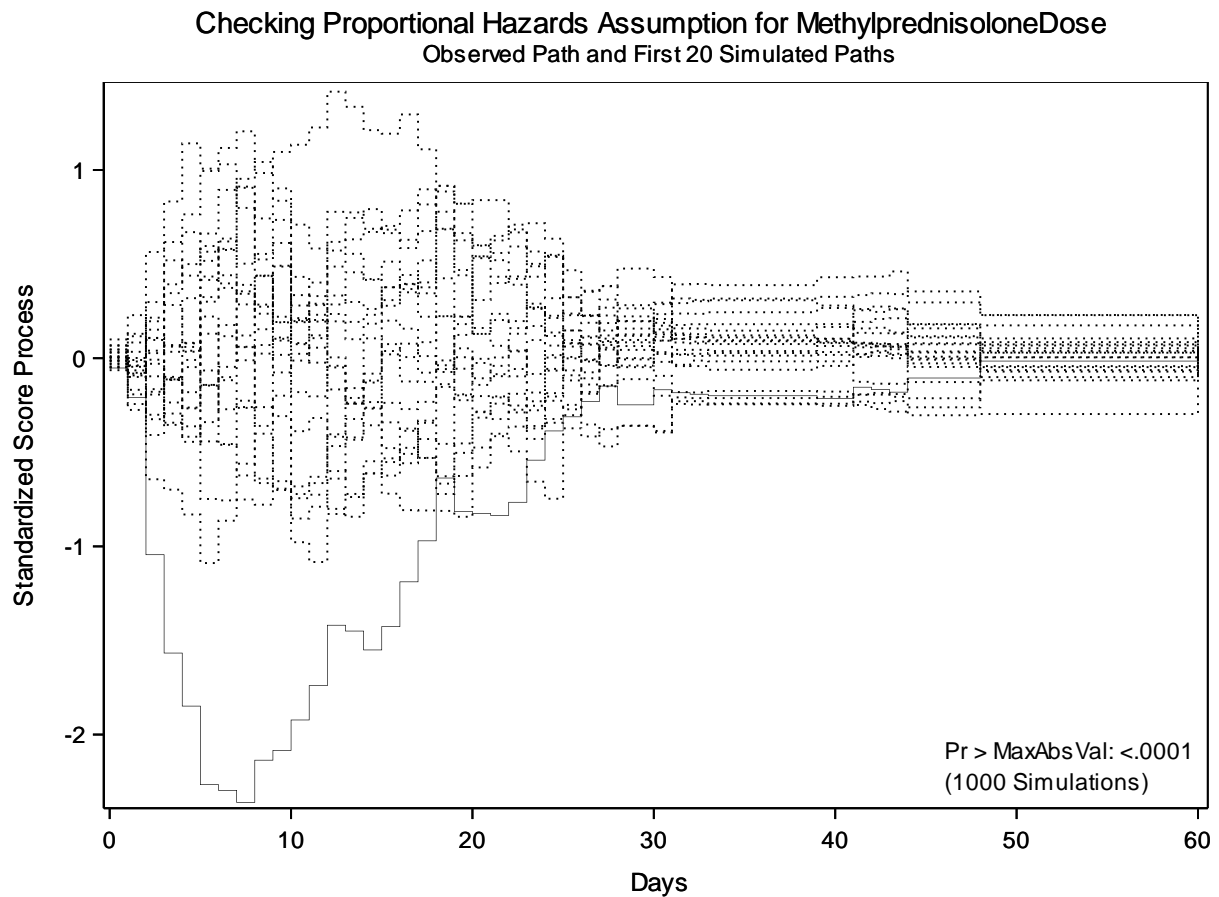


In the following, we examined the proportional assumption using a formal test of Supremum test of proportionality, Lin, Wei, Ying (1993). Table S3 is a summary of all the covariates that were indicated to failed to satisfy the proportional based on the Supremum test. Tables S4 – S10 contain the results of the test for each variable included in the propensity matched cohort.

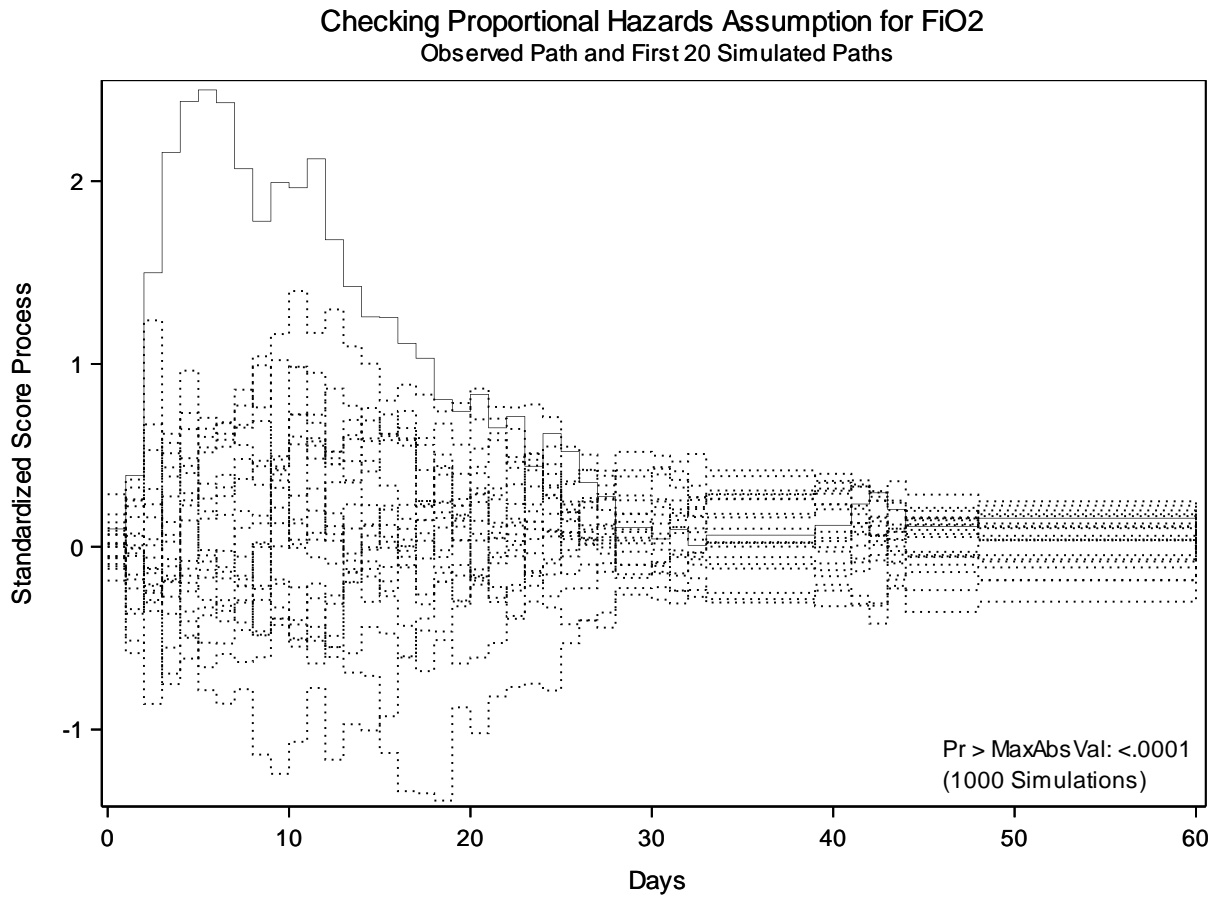
**Figure S13.** Plot of observed standardized score process of methylprednisolone vs. 20 simulated realizations. The plot shows that with the first 20 of 1,000 simulated realizations (depicted by thin dotted line) conducted here, the observed MP process (depicted by the thick solid line) exhibited significant deviation from the paths of simulations within the first 20 days since the COVID-19 admission and then thereafter the MP process was more typical with simulated realization. Over the 1000 simulated realization, the supremum test reported an absolute maximum value of 2.2103 with p-value of  $<0.0001$ . Thus, the test indicated that methylprednisolone administration significantly violated the proportional hazards assumption.



**Figure S14.** Plot of observed standardized score process of methylprednisolone (MP) dose level (NMP, LD, HD) vs. 20 simulated realizations. The plot shows that with the first 20 of 1,000 simulated realizations (depicted by thin dotted line) conducted here, the observed MP dose process (depicted by the thick solid line) exhibited significant deviation from the paths of simulations within the first 20 days since the COVID-19 admission and then thereafter the MP dose process was more typical with simulated realizations. Over the 1000 simulated realization, the supremum test reported an absolute maximum value of 2.360 with p-value of  $<0.0001$ . Thus, the test indicated that methylprednisolone dose level significantly violated the proportional hazards assumption.



**Figure S15.** Plot of observed standardized score process of  $\text{FiO}_2$  (%) vs. 20 simulated realizations. The plot shows that with the first 20 of 1,000 simulated realizations (depicted by thin dotted line) conducted here, the observed  $\text{FiO}_2$  process (depicted by the thick solid line) exhibited significant deviation from the paths of simulations within the first 20 days since the COVID-19 admission and then thereafter the  $\text{FiO}_2$  process was more typical with simulated realizations. Over the 1000 simulated realization, the supremum test reported an absolute maximum value of 2.4993 with p-value of  $<0.0001$ . Thus, the test indicated that  $\text{FiO}_2$  level significantly violated the proportional hazards assumption.



**Table S3.** Assessment of the Proportional Hazards Assumptions in Baseline Characteristics in COVID-19 Patients

Variable	Max Abs Value	Replications	Seed	P-Value
<b>Nursing Home</b>	<b>1.4886</b>	<b>1000</b>	<b>19</b>	<b>0.0110</b>
<b>Anosmia or Ageusia</b>	<b>0.0030</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
<b>WBC lower</b>	<b>2.3013</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
<b>Creatinine high</b>	<b>1.2404</b>	<b>1000</b>	<b>19</b>	<b>0.0400</b>
<b>Respiratory Rate high</b>	<b>1.3106</b>	<b>1000</b>	<b>19</b>	<b>0.0420</b>
<b>Hydroxychloroquine</b>	<b>1.6164</b>	<b>1000</b>	<b>19</b>	<b>0.0020</b>
<b>Methylprednisolone</b>	<b>2.2103</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
<b>HD/LD/No Methylprednisolone</b>	<b>2.3601</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
<b>FiO<sub>2</sub></b>	<b>2.4993</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
<b>qSOFA</b>	<b>1.5330</b>	<b>1000</b>	<b>19</b>	<b>0.0200</b>
<b>Calcium</b>	<b>1.3128</b>	<b>1000</b>	<b>19</b>	<b>0.0360</b>
<b>Initial BP (diastolic)</b>	<b>1.4722</b>	<b>1000</b>	<b>19</b>	<b>0.0330</b>

Supremum Test for Proportional Hazard Assumption. Any P<0.05 was Statistically Significant.

**Table S4.** Assessment of the Proportional Hazards Assumptions for the Demographic and comorbidities

Variable	Max Abs Value	Replications	Seed	P-Value
Sex	0.8227	1000	19	0.3490
Older age	1.0353	1000	19	0.1520
Obesity status	1.1676	1000	19	0.0660
Form current Smoker	0.6363	1000	19	0.6040
Is Smoker	0.5641	1000	19	0.7890
<b>Nursing Home</b>	<b>1.4886</b>	<b>1000</b>	<b>19</b>	<b>0.0110</b>
Fever	0.3243	1000	19	0.9880
SOB	1.0332	1000	19	0.1350
Cough	0.9889	1000	19	0.1750
AMS Symptoms	1.1986	1000	19	0.0530
GI	0.6098	1000	19	0.6500
<b>Anosmia or Ageusia</b>	<b>0.0030</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
Symptoms>7days	0.5481	1000	19	0.7380
Duration symptom Cat	0.8762	1000	19	0.2280
Diabetes	0.6145	1000	19	0.6330
COPD_O2	0.6974	1000	19	0.4280
COPD	0.2846	1000	19	0.9930
Asthma	0.5324	1000	19	0.7420
COPD/asthma	0.3837	1000	19	0.9530
Hypertension	0.9271	1000	19	0.2310
Cancer	1.0278	1000	19	0.1280
Coronary	0.8326	1000	19	0.3160
Coronary Stroke	1.1629	1000	19	0.0920
Coronary Heart	0.9956	1000	19	0.1510
Coronary Arrhythmia	0.8273	1000	19	0.2920



Variable	Max Abs Value	Replications	Seed	P-Value
Renal Failure	0.5449	1000	19	0.7580
Renal Failure Dialysis	0.6128	1000	19	0.5880
Rheumatic disease disorder	0.6623	1000	19	0.5470

Supremum Test for Proportional Hazard Assumption. Any  $P < 0.05$  was Statistically Significant.

**Table S5.** Assessment of the Proportional Hazards Assumptions for the dichotomized lab values and respiratory rate

Variable	Max Abs Value	Replications	Seed	P-Value
<b>WBC lower</b>	<b>2.3013</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
HBG lower norm	1.1560	1000	19	0.0730
Platelet lower norm	0.6383	1000	19	0.5980
Abs lymphocyte lower norm	0.6654	1000	19	0.4550
IL-6 high	1.1596	1000	19	0.0830
CRP d1 High	0.9503	1000	19	0.2040
Ferritin high	0.5388	1000	19	0.7860
D-dimer categ	0.9539	1000	19	0.2180
<b>Creatinine high</b>	<b>1.2404</b>	<b>1000</b>	<b>19</b>	<b>0.0400</b>
<b>Respiratory Rate high</b>	<b>1.3106</b>	<b>1000</b>	<b>19</b>	<b>0.0420</b>

Supremum Test for proportional hazard assumption. Any  $p < 0.05$  was statistically significant.

**Table S6.** Assessment of the Proportional Hazards Assumptions for therapy for COVID-19

Variable	Max Abs Value	Replications	Seed	P-Value
<b>HCQ</b>	<b>1.6164</b>	<b>1000</b>	<b>19</b>	<b>0.0020</b>
Azithromycin	0.8226	1000	19	0.3600
HCQ and AZ	0.7439	1000	19	0.2570
Remdesivir	0.7195	1000	19	0.4200
Tocilizumab	0.7093	1000	19	0.4830
SAR	0.8885	1000	19	0.2530
Convalescent Plasma	0.4901	1000	19	0.3390
<b>Methylprednisolone</b>	<b>2.2103</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
<b>HD/LD/No Methylprednisolone</b>	<b>2.3601</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>

Supremum Test for proportional hazard assumption. Any  $p < 0.05$  was statistically significant

**Table S7.** Assessment of the Proportional Hazards Assumptions for clinical presentation parameters

Variable	Max Abs Value	Replications	Seed	P-Value
Elevated LFTs	0.8344	1000	19	0.3650
Low Oxygen	0.9414	1000	19	0.2120
Supplemental Oxygen	0.8402	1000	19	0.3030
<b>FiO<sub>2</sub></b>	<b>2.4993</b>	<b>1000</b>	<b>19</b>	<b>&lt;.0001</b>
<b>qSOFA</b>	<b>1.5330</b>	<b>1000</b>	<b>19</b>	<b>0.0200</b>
Fever Temp	0.7363	1000	19	0.5400
Intubated	1.0596	1000	19	0.1160
Mechanical ventilation	0.5595	1000	19	0.5940

Supremum Test for proportional hazard assumption. Any  $p < 0.05$  was statistically significant.

**Table S8.** Assessment of the Proportional Hazards Assumptions for labs (continuous) form

Variable	Max Abs Value	Replications	Seed	P-Value
White Blood Cells	0.7495	1000	19	0.1300
Abs. neutrophil count	0.9530	1000	19	0.2840
Abs. lymphocyte count	0.9140	1000	19	0.2870
Abs. Neutrophil/Lymphocyte Ratio	0.8075	1000	19	0.3350
Platelets	0.8027	1000	19	0.4820
HGB	1.0019	1000	19	0.3350
LDH	0.5495	1000	19	0.8100
Ferritin	0.9932	1000	19	0.1850
D-dimer	0.4179	1000	19	0.8120
C-reactive Protein	0.6009	1000	19	0.6370
Troponin	0.6315	1000	19	0.3740
BNP	0.8043	1000	19	0.0980
Creatinine	0.8413	1000	19	0.1350
AST	0.5009	1000	19	0.5200
ALT	0.4692	1000	19	0.6730
Bilirubin	0.1955	1000	19	0.5030

Supremum Test for proportional hazard assumption. Any  $p < 0.05$  was statistically significant.

**Table S9.** Assessment of the Proportional Hazards Assumptions for the inflammatory markers

Variable	Max Abs Value	Replications	Seed	P-Value
IL-6 on Admission	0.4438	1000	19	0.6970
IL-6 Recent	0.4438	1000	19	0.6970
CK	0.7009	1000	19	0.1930
La	0.8184	1000	19	0.3190
Potassium	0.8724	1000	19	0.2810
Magnesium	0.6025	1000	19	0.5370
Phosphate	0.4909	1000	19	0.3360
<b>Calcium</b>	<b>1.3128</b>	<b>1000</b>	<b>19</b>	<b>0.0360</b>
Sodium	0.3766	1000	19	0.8310
BUN	0.4980	1000	19	0.5620
HCT	0.7023	1000	19	0.6600
Glucose	0.4796	1000	19	0.5520
Total bilirubin	0.3156	1000	19	0.7450

Supremum Test for proportional hazard assumption. Any  $p < 0.05$  was statistically significant.

**Table S10.** Assessment of the Proportional Hazards Assumptions for the vitals

Variable	Max Abs Value	Replications	Seed	P-Value
Initial temperature	0.5519	1000	19	0.7350
Initial Heart rate	0.3960	1000	19	0.9890
Initial BP (Systolic)	0.7093	1000	19	0.6500
<b>Initial BP (diastolic)</b>	<b>1.4722</b>	<b>1000</b>	<b>19</b>	<b>0.0330</b>
Mean arterial pressure	1.2078	1000	19	0.1220
Initial Respiratory Rate	0.4505	1000	19	0.5730
Height (cm)	0.5232	1000	19	0.7760
Weight(kg)	0.9904	1000	19	0.1310
BMI kg/m <sup>2</sup>	1.0447	1000	19	0.1000
Diagnosis age years	1.3620	1000	19	0.0500

Supremum Test for proportional hazard assumption. Any  $p < 0.05$  was statistically significant.

**Table S11.** Univariate\* Cox Regression Analysis of In-hospital Mortality in COVID-19 Patients

\* univariate associations were reported for covariate that satisfied the proportional hazard assumption with since admission to COVID-19 hospitalization. Variables which demonstrated that the NPH assumption was violated were adjusted by inclusion of an interaction of FiO<sub>2</sub> and time, and FiO<sub>2</sub> in the model.

Comparison Effect	HR (95% CI)	P-Value
Male vs Female	1.20 (0.93, 1.56)	0.1691
<b>Age&gt;60 vs &lt;60</b>	<b>2.83 (2.05, 3.91)</b>	<b>&lt;.0001</b>
Current vs Non-Smoker	0.62(0.29, 1.32)	0.2154
Former vs Current Smoker	1.21(0.91, 1.61)	0.1934
<b>Unknown Race vs Asian</b>	<b>2.08(1.11, 3.89)</b>	<b>0.0224</b>
Black vs Asian	1.00(0.56, 1.79)	0.9926
Other Race vs Asian	1.12(0.65, 1.91)	0.6887
White vs Asian	1.33(0.81, 2.20)	0.2651
Academic vs Community Hospital	1.18 (0.91, 1.52)	0.2105
<b>Nursing Home vs Home</b>	<b>2.81(1.99, 3.96)</b>	<b>&lt;.0001</b>
<i>Symptoms</i>		
Fever vs None	0.88 (0.67, 1.15)	0.3445
SOB vs None	1.18 (0.91, 1.53)	0.2233
Cough vs None	0.79 (0.61, 1.01)	0.0641
<b>AMS vs None</b>	<b>3.14(2.32, 4.26)</b>	<b>&lt;.0001</b>
<b>GI vs None</b>	<b>0.66(0.47, 0.93)</b>	<b>0.0185</b>
<b>Anosmia or Ageusia vs None</b>	NA	<b>&lt;.0001</b>
<b>Duration of Symptoms PTA &gt; 7 vs ≤ 7 days</b>	<b>0.61 (0.41, 0.91)</b>	<b>0.0143</b>
Diabetes vs None	1.06 (0.82, 1.37)	0.6503
<b>COPD vs None</b>	<b>2.44 (1.64, 3.63)</b>	<b>&lt;.0001</b>
Asthma vs None	0.89 (0.56,1.41)	0.6042
<b>COPD/Asthma vs None</b>	<b>1.49(1.07, 2.05)</b>	<b>0.0169</b>
<b>Hypertension vs None</b>	<b>2.12 (1.60, 2.81)</b>	<b>&lt;.0001</b>
<b>Cancer vs None</b>	<b>2.08 (1.46, 2.97)</b>	<b>&lt;.0001</b>
<b>CAD vs None</b>	<b>2.09 (1.56, 2.79)</b>	<b>&lt;.0001</b>
<b>CVA vs None</b>	<b>2.24 (1.44, 3.50)</b>	<b>0.0004</b>
<b>CHF vs None</b>	<b>2.12 (1.41, 3.21)</b>	<b>0.0004</b>
<b>Arrhythmia vs None</b>	<b>2.07 (1.43, 2.98)</b>	<b>0.0001</b>
<b>Renal Failure vs None</b>	<b>1.95 (1.37, 2.78)</b>	<b>0.0002</b>
Dialysis vs None	0.74 (0.39, 1.43)	0.3726
<i>Presentations Characteristics</i>		
Elevated LFTS vs None	1.03 (0.80, 1.33)	0.8142
Low Oxygen Saturation vs None	0.99 (0.77, 1.28)	0.9307
<b>Mechanical Ventilation vs None</b>	<b>1.62 (1.16, 2.27)</b>	<b>0.0051</b>
Non-Mechanical Ventilation Oxygen Support Vs None	0.98 (0.64, 1.50)	0.9233
qSOFA 3 vs 0	10.23 (5.00, 20.96)	<.0001
<b>qSOFA 2 vs 0</b>	<b>3.64 (2.41, 5.50)</b>	<b>&lt;.0001</b>

Comparison Effect	HR (95% CI)	P-Value
<b>qSOFA 1 vs 0</b>	<b>1.42 (1.07, 1.90)</b>	<b>0.0169</b>
<b>Hydroxychloroquine vs None</b>	<b>0.41 (0.30, 0.56)</b>	<b>&lt;.0001</b>
<b>Azithromycin vs None</b>	<b>0.64 (0.49, 0.84)</b>	<b>0.0012</b>
HCQ and Az vs None	0.89 (0.19, 4.26)	0.8860
Remdesivir vs None	0.78 (0.34, 1.81)	0.5637
<b>Tocilizumab vs None</b>	<b>0.68 (0.47, 0.98)</b>	<b>0.0407</b>
Convalescent Plasma vs None	0.23 (0.03, 1.74)	0.1558
<b>Methylprednisolone</b>		
<i>Dose</i>		
<b>MP vs NMP</b>	<b>0.44 (0.33, 0.60)</b>	<b>&lt;.0001</b>
<b>HD MP vs NMP</b>	<b>0.61 (0.44, 0.85)</b>	<b>0.0033</b>
<b>LD MP vs NMP</b>	<b>0.34 (0.24, 0.48)</b>	<b>&lt;.0001</b>
<i>Level of Oxygen Support Vs MP Dose</i>		
No oxygen support in HD MP vs NMP	0.96 (0.49, 1.86)	0.8940
No oxygen support in LD MP vs NMP	0.25 (0.10, 0.62)	<b>0.0028</b>
Oxygen support in HD MP vs NMP	0.50 (0.24, 1.06)	0.0701
Oxygen support in LD MP vs NMP	0.08 (0.02, 0.28)	<b>&lt;.0001</b>
Mechanical Ventilation in HD MP vs NMP	0.39 (0.23, 0.65)	<b>0.0003</b>
<b>Mechanical Ventilation in LD MP vs NMP</b>	<b>0.34 (0.20, 0.57)</b>	<b>&lt;.0001</b>
<i>Duration</i>		
<b>MP ≤ 7 vs &gt; 7 days</b>	<b>1.86 (1.36, 2.56)</b>	<b>&lt;.0001</b>
<b>HD MP ≤ 7 vs &gt; 7 days</b>	<b>2.00 (1.25, 3.20)</b>	<b>0.0039</b>
<b>HD vs LD MP ≤ 7 days</b>	<b>1.73 (1.11, 2.70)</b>	<b>0.0157</b>
<b>HD MP ≤ 7 days vs LD MP &gt; 7 days</b>	<b>4.01 (2.45, 6.57)</b>	<b>&lt;.0001</b>
HD MP ≤ 7 days vs NMP	0.82 (0.55, 1.20)	0.3095
HD MP > 7 days vs LD MP ≤ 7 days	0.87 (0.55, 1.35)	0.5364
<b>HD MP &gt; 7 days vs LD MP &gt; 7 days</b>	<b>2.01 (1.22, 3.30)</b>	<b>0.0061</b>
<b>HD MP &gt; 7 days vs NMP</b>	<b>0.41 (0.26, 0.62)</b>	<b>&lt;.0001</b>
<b>LD MP ≤ 7 vs &gt; 7 days</b>	<b>2.32 (1.43, 3.75)</b>	<b>0.0006</b>
<b>LD MP ≤ 7 days vs NMP</b>	<b>0.47 (0.32, 0.71)</b>	<b>0.0002</b>
<b>LD MP &gt; 7 days vs NMP</b>	<b>0.20 (0.13, 0.32)</b>	<b>&lt;.0001</b>
<i>Timing from Onset of Symptoms</i>		
<b>&gt;7-14 days vs ≤ 7 days</b>	<b>0.70 (0.49, 0.99)</b>	<b>0.0462</b>
<b>&gt;14 days vs ≤ 7 days</b>	<b>0.32 (0.16, 0.63)</b>	<b>0.0010</b>

HR = Hazard Ratio; CI = Confidence Interval; SOB = Shortness of Breath; AMS = Altered Mental Status; GI = Gastrointestinal Symptoms; PTA = Prior to admission; COPD = Chronic Obstructive Disease; CAD = Coronary Artery Disease; CVA = Cerebrovascular Accident; CHF = Congestive Heart Failure; LFTs = elevated liver function tests; SOFA = Sequential Organ Failure Assessment; HCQ = Hydroxychloroquine; AZ = Azithromycin; MP = Methylprednisolone; HD MP = High Dose Methylprednisolone; LD MP = Low Dose Methylprednisolone

**Table S12.** Multivariable Risk of In-hospital mortality in COVID-19 patients with/without methylprednisolone *Model 1* included interaction of FiO<sub>2</sub> and time to adjust for interaction between time and risk factors including methylprednisolone, nursing home, coronary artery disease, supplemental oxygen in mechanical ventilation form vs none, supplemental oxygen in non-mechanical ventilation form vs none, hydroxychloroquine, and azithromycin.

Variable	Category	HR (95% CI)	P-Value
<b>Methylprednisolone</b>	<b>Methylprednisolone vs None</b>	<b>0.40 (0.27, 0.59)</b>	<b>&lt;.0001</b>
<b>Nursing home</b>	<b>Yes vs. No</b>	<b>3.08 (1.94, 4.89)</b>	<b>&lt;.0001</b>
<b>Coronary Artery Disease</b>	<b>Yes vs. No</b>	<b>2.12 (1.38, 3.27)</b>	<b>0.0006</b>
<b>Supplemental Oxygen</b>	<b>Mechanical-Ventilation vs. None</b>	<b>2.87 (1.64, 5.02)</b>	<b>0.0002</b>
Supplemental Oxygen	Non-mechanical Ventilation vs. None	1.11 (0.60, 2.05)	0.7483
Hydroxychloroquine	Yes vs. No	0.67 (0.43,1.02)	0.0644
<b>Azithromycin</b>	<b>Yes vs. No</b>	<b>0.64 (0.44, 0.93)</b>	<b>0.0183</b>

HR, Hazard Ratio; CI, confidence interval

Risk of in-hospital mortality by nonproportional hazard (NPH)

Cox Regression model. Any p<0.05 was statistically significant.

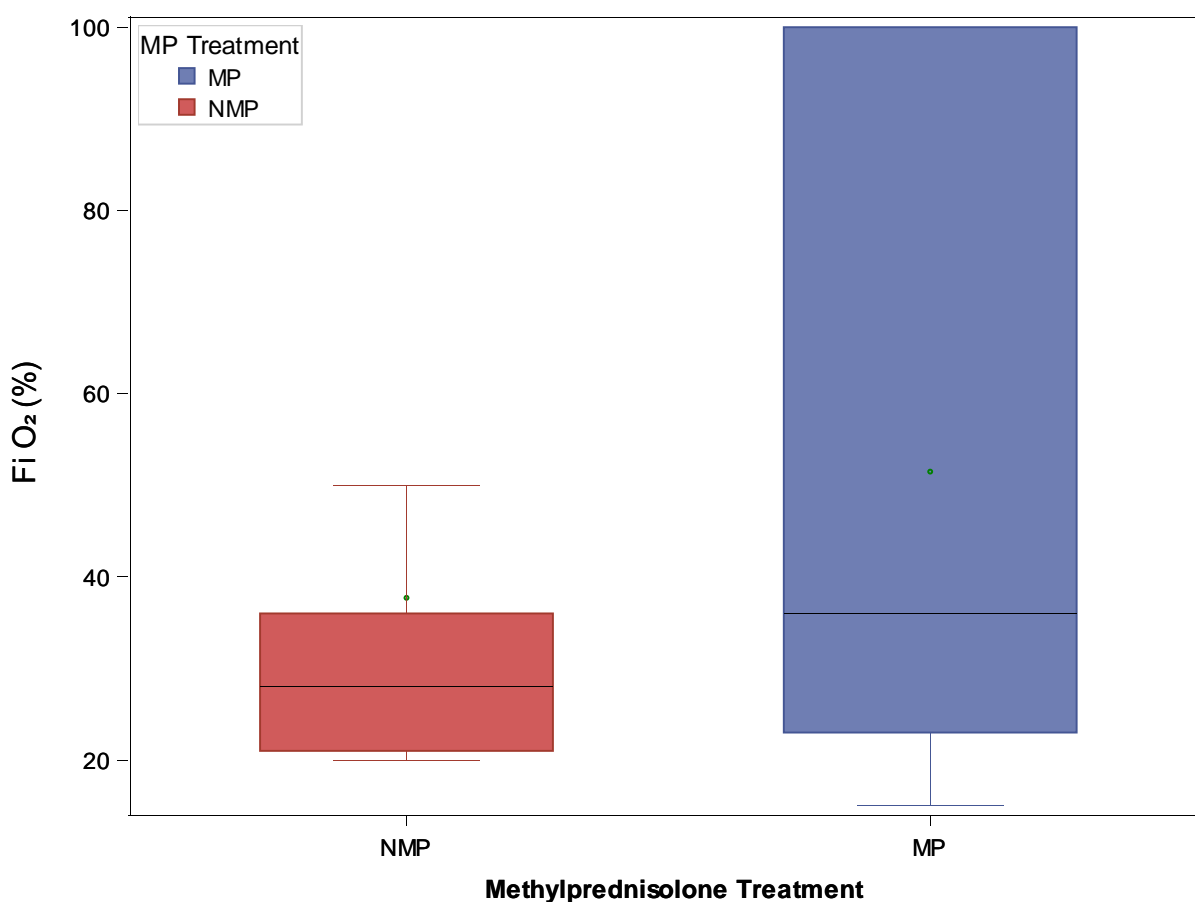


**Table S13.** Multivariable Risk of In-hospital mortality in COVID-19 patients with HD, LD and No methylprednisolone. *Model 2* included interaction of FiO2 and time to adjust for interaction between time and risk factors including methylprednisolone dose {High Dose(HD),Low Dose (LD), None}, nursing home, coronary artery disease, supplemental oxygen in mechanical ventilation form vs none, supplemental oxygen in non-mechanical ventilation form vs none, hydroxychloroquine, and azithromycin.

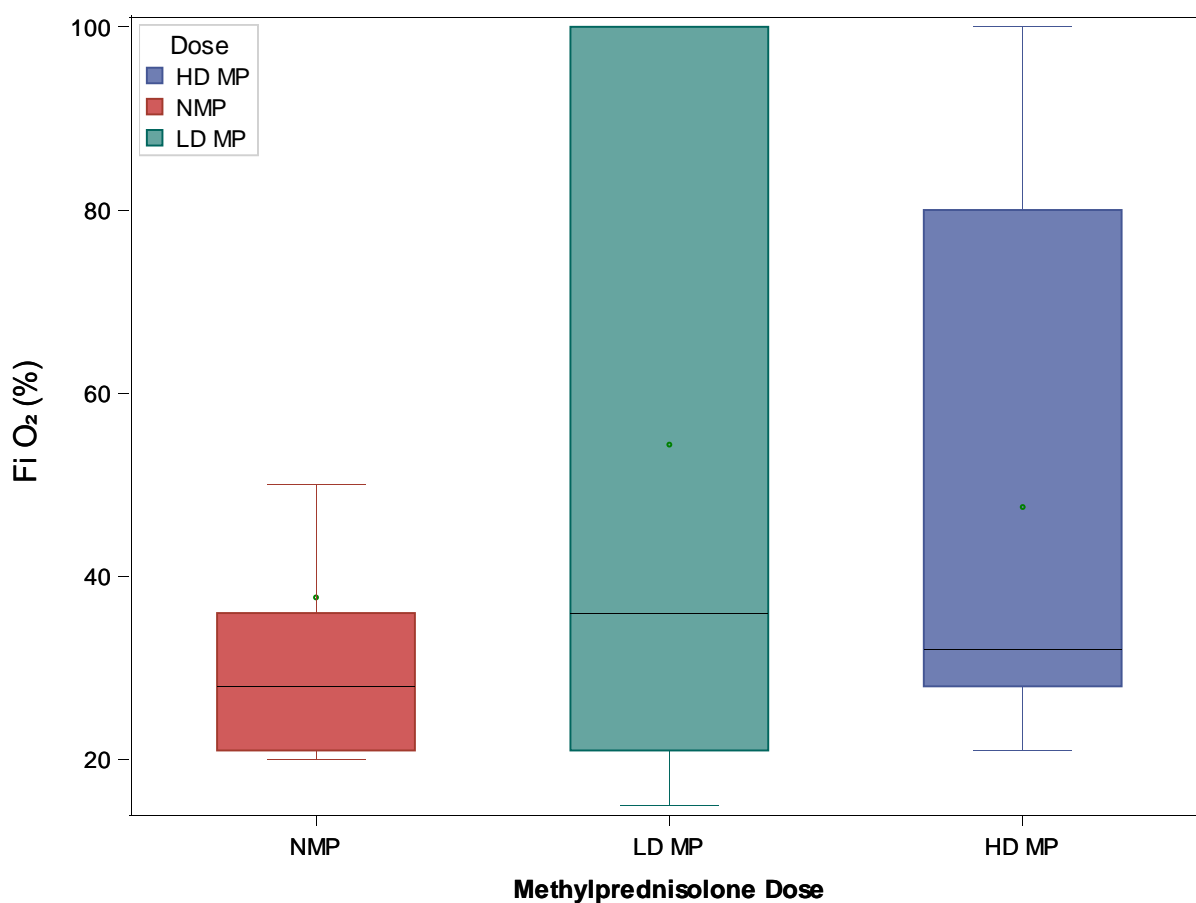
Variable	Category	HR (95% CI)	P-Value
<b>Methylprednisolone Dose</b>	<b>HD Methylprednisolone vs. None</b>	<b>0.48 (0.30, 0.77)</b>	<b>0.0025</b>
<b>Methylprednisolone Dose</b>	<b>LD Methylprednisolone vs. None</b>	<b>0.35 (0.22, 0.53)</b>	<b>&lt;.0001</b>
<b>Nursing home</b>	<b>Yes vs. No</b>	<b>2.95 (1.83, 4.76)</b>	<b>&lt;.0001</b>
<b>Coronary Artery Disease</b>	<b>Yes vs. No</b>	<b>2.22 (1.44, 3.42)</b>	<b>0.0003</b>
<b>Supplemental Oxygen</b>	<b>Mechanical-Ventilation vs. None</b>	<b>2.77(1.58, 4.86)</b>	<b>0.0004</b>
Supplemental Oxygen	Non-mechanical Ventilation vs. None	1.13 (0.61, 2.09)	0.6992
Hydroxychloroquine	Yes vs. No	0.67 (0.44,1.02)	0.0642
<b>Azithromycin</b>	<b>Yes vs. No</b>	<b>0.66 (0.45, 0.95)</b>	<b>0.0262</b>

HR, Hazard Ratio; CI, confidence interval. Risk of in-hospital mortality by nonproportional hazard (NPH) Cox Regression model. Any p<0.05 was statistically significant.

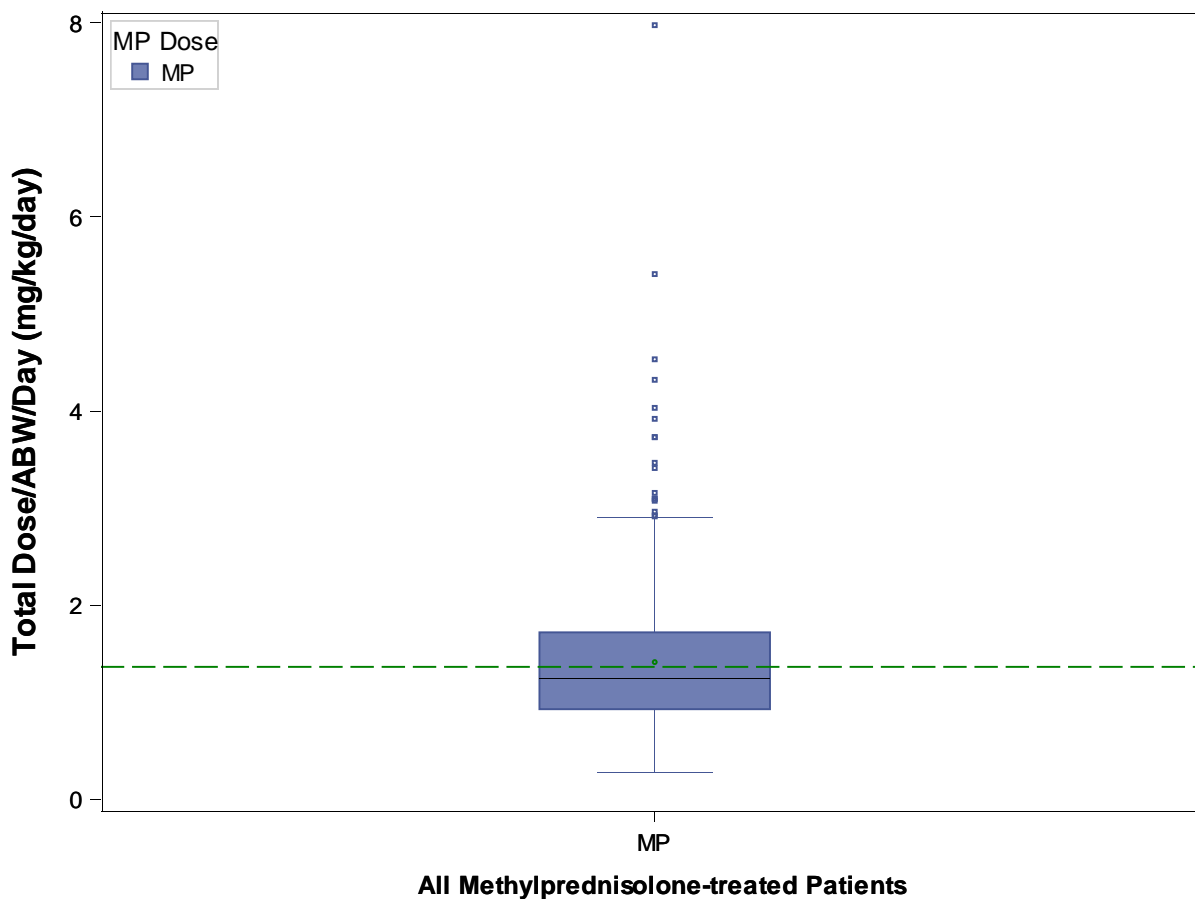
**Figure S16.** Boxplots of fraction of inspired oxygen ( $\text{FiO}_2$ ) reported on admission in COVID-19 patients who were not treated with methylprednisolone and COVID-19 patients who received methylprednisolone. In each boxplot, the horizontal line in the middle indicates the median, the bottom edge of the box is the 25<sup>th</sup> percentile and the top edge of the box is the 75<sup>th</sup> percentile of  $\text{FiO}_2$ . The lower endpoints of the whiskers on each side of the box indicate the minimum and maximum value. The patients who did not receive methylprednisolone reported median  $\text{FiO}_2$  value of 28% (IQR: 21%- 36%) with a range of 20% to 100% from 368 of the 383 patients. The patients who received methylprednisolone reported median  $\text{FiO}_2$  value of 36% (IQR: 23% - 100%) with a range of 15% to 100% from 354 of the 380 patients. Analysis of  $\text{FiO}_2$  differences between matched patients indicated the median of 4.0% (IQR 0% to 35%) MP vs NMP was statistically significant (Wilcoxon signed rank test  $P < .0001$ ).



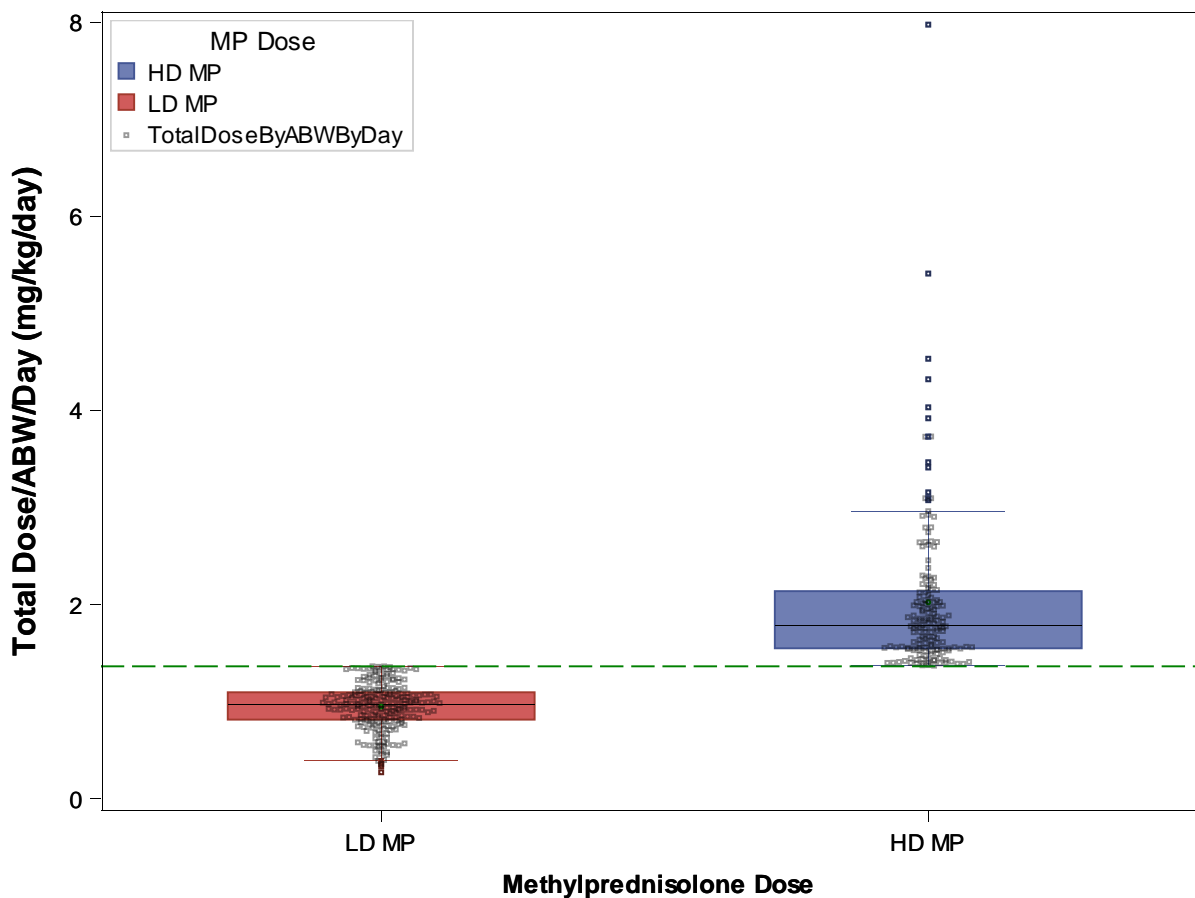
**Figure S17.** Boxplots of fraction of inspired oxygen (FiO<sub>2</sub>) reported on admission in COVID-19 patients who were not treated with methylprednisolone (NMP) and COVID-19 patients who received LD methylprednisolone (LD MP) and HD methylprednisolone (HD MP). LD MP was defined as < 1.36 mg/kg/day and HD MP was defined as ≥ 1.36 mg/kg/day. In each boxplot, the horizontal line in the middle indicates the median, the bottom edge of the box is the 25<sup>th</sup> percentile and the top edge of the box is the 75<sup>th</sup> percentile of FiO<sub>2</sub>. The lower endpoints of the whiskers on each side of the box indicate the minimum and maximum value. The patients who did not receive methylprednisolone reported median FiO<sub>2</sub> value of 28% (IQR: 21%- 36%) with a range of 20% to 100% from 368 of the 383 patients. The patients who received LD MP reported median FiO<sub>2</sub> value of 36% (IQR: 21% - 100%) with a range of 15% to 100% from 203 of the 380 patients. The patients who received HD MP reported median FiO<sub>2</sub> value of 32% (IQR: 28% - 80%) with a range of 21% to 100% from 151 of the 380 patients. Analysis of FiO<sub>2</sub> differences between matched patients indicated the median of 4.0% (IQR 0% to 64%) LD MP vs NMP was statistically significant (Wilcoxon signed rank test P<.0001). Analysis of FiO<sub>2</sub> differences between matched patients indicated the median of 7.0% (IQR 0% to 19%) HD MP vs NMP was statistically significant (Wilcoxon signed rank test P<.0001).



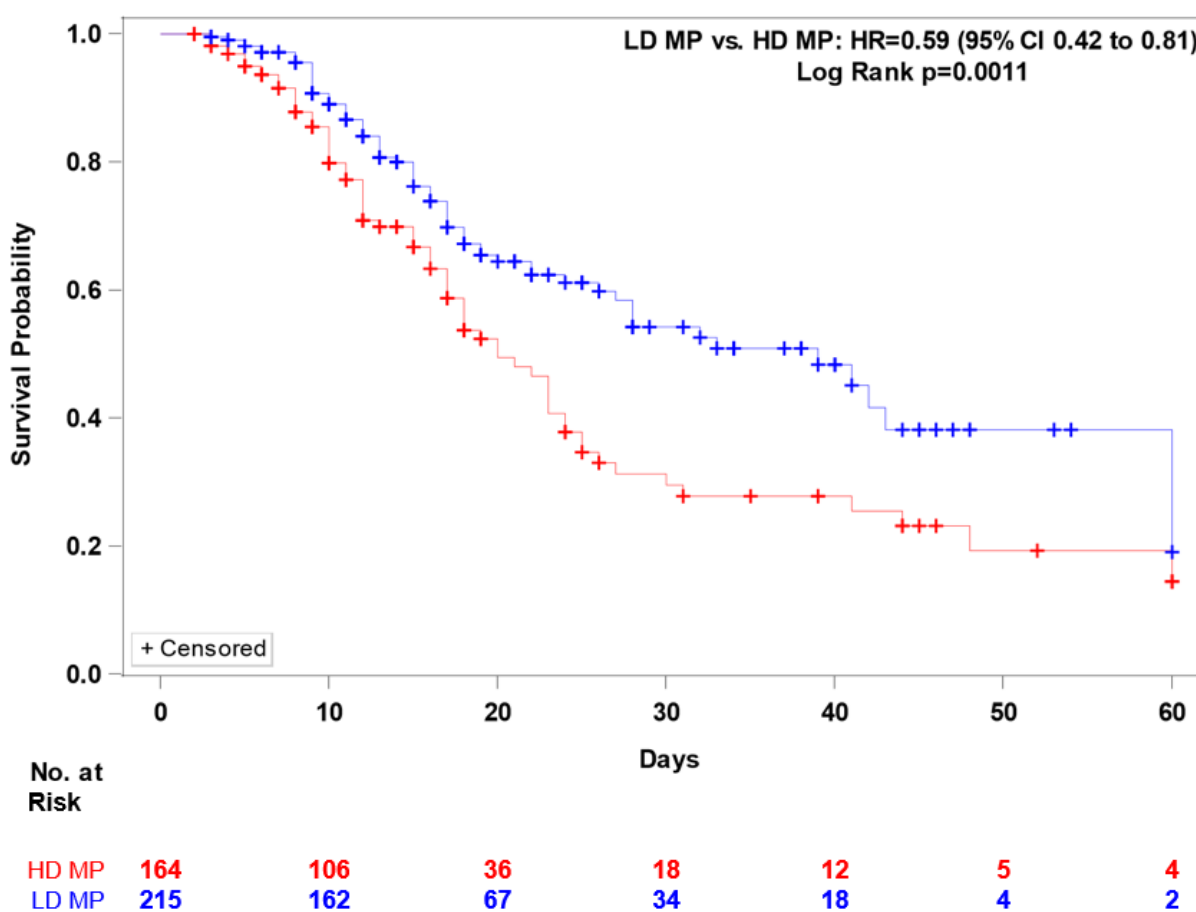
**Figure S18.** Boxplot of Total Dose/Absolute Body Weight/Day in hospitalized COVID-19 patients who received Methylprednisolone (N=380). In the box plot above, the horizontal line in the middle indicates the median, the bottom edge of the box is the 25th percentile and the top edge of the box is the 75th percentile of Total Dose/ABW/Day. The lower endpoints of the whiskers on each side of the box indicate the minimum and maximum value. The green dashed line at Total Dose/ABW/Day of 1.36 depicts the cut-off value that was determined by the Youden Index Method. The total dose/ABW/day in the all methylprednisolone treated patients had a median of 1.25 mg/kg/day (IQR: 0.93 – 1.72 mg/kg/day), range 0.27 – 7.98 mg/kg/day. The cut-off value of total dose/ABW/day of 1.36 mg/kg/day against the mortality event had an area under ROC curve of 56.8% (95% CI 51.7% to 62.0%), which is not very high. Further the cut-off value had a sensitivity of 51.8% and specificity of 62.0% in determining patients who are at higher risk for in-hospitality mortality than lower risk. Thus, while this cutoff value should not be used as a reference level since administration of methylprednisolone moderate-severe COVID-19 was not employed as the main therapy in an clinically designed trial, but rescue therapy, it provides us with a measure of predictive capability that underpinned its prescription during new pandemic.



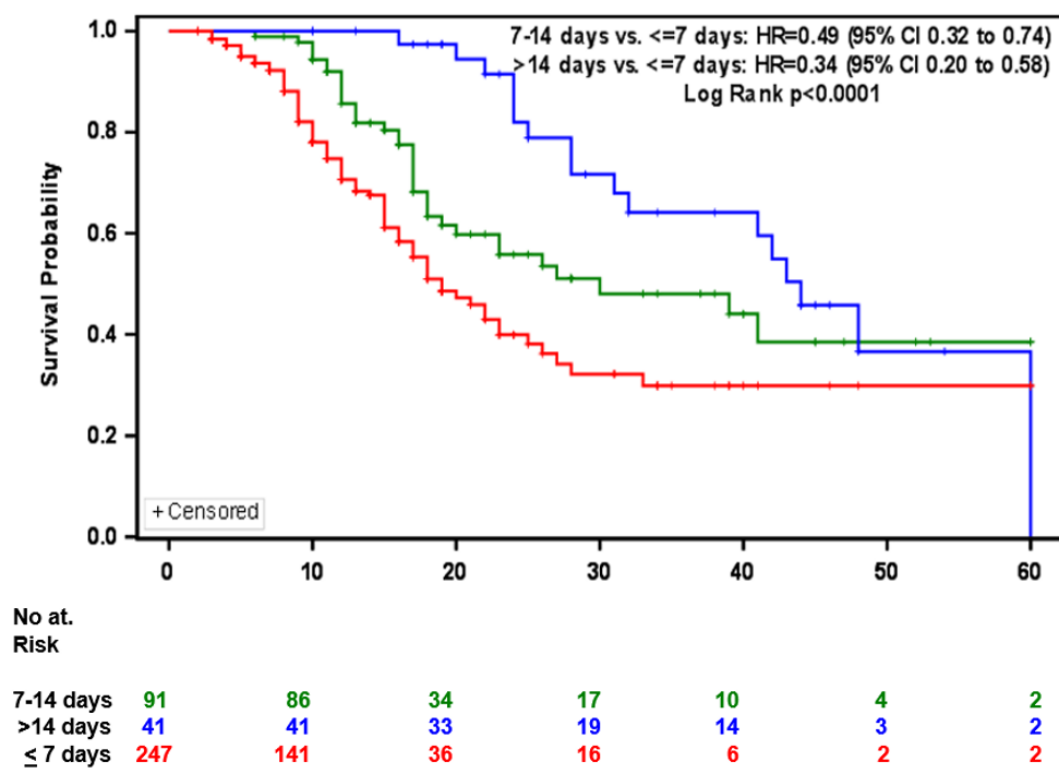
**Figure S19.** Boxplot of Total Dose/Absolute Body Weight/Day in hospitalized COVID-19 patients who received LD Methylprednisolone (N=216) and HD Methylprednisolone (N=164). In each boxplot, the horizontal line in the middle indicates the median, the bottom edge of the box is the 25th percentile and the top edge of the box is the 75th percentile of Total Dose/ABW/Day. The lower endpoints of the whiskers on each side of the box indicate the minimum and maximum value. The green dashed line at Total Dose/ABW/Day of 1.36 depicts the cut-off value that was determined by the Youden Index Method. The total dose/ABW/day in the LD methylprednisolone treated patients had a median of 0.98 mg/kg/day (IQR: 0.82 – 1.10 mg/kg/day), range 0.27 – 1.36 mg/kg/day. The total dose/ABW/day in the HD methylprednisolone treated patients had a median of 1.79 mg/kg/day (IQR: 1.55 – 2.14 mg/kg/day), range 1.37 – 7.98 mg/kg/day.



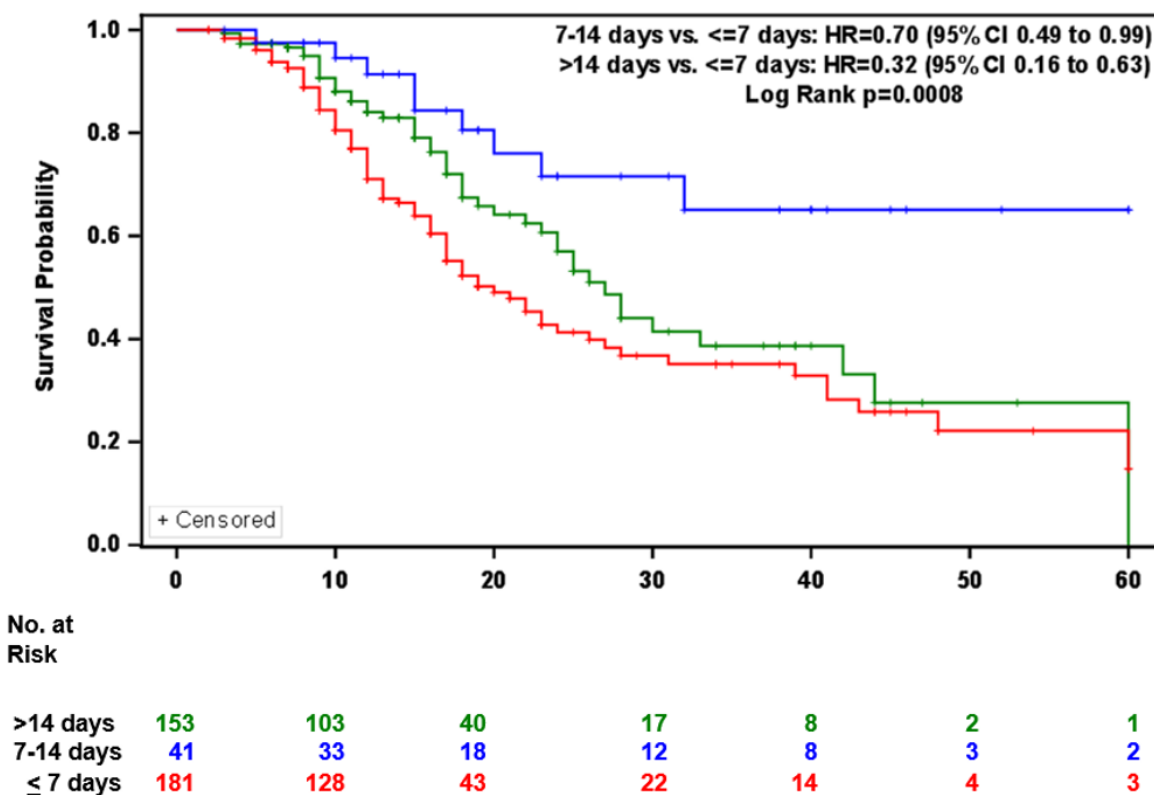
**Figure S20.** Kaplan-Meier Plot of in-hospital survival for low dose methylprednisolone (LD MP) and high dose methylprednisolone (HD MP) treated cohorts in admitted COVID-19 patients. Out of the 215 patients in the LD MP cohort, 69 (31.9%) expired during COVID-19 hospital stay. Out of the 164 patients in the HD MP cohort, 74 (55.2%) expired during COVID-19 hospital stay. 30-Day and 60-Day In-hospital survival for the LD MP cohort were 54.2% (95% CI 44.8% to 63.5%) and 19.1% (95% CI 1.1% to 51.4%), respectively. 30-Day and 60-Day In-hospital survival for the HD MP cohort were 29.6% (95% CI 19.8% to 40.4%) and 14.4% (95% CI 5.0% to 27.9%), respectively. The difference in In-hospital survival between the NMP (median=25.0 days (95% CI 22.0 to 32.0 days)] and LD MP (median =39.0 days (95% CI 27.0 to N/A days)] and HD MP (median =20.0 days (95% CI 17.0 to 24 days)] was statistically significant (Log-rank P=0.0011). These data indicate there was survival benefit for the patients that were treated with LD MP throughout the Day 60 follow-up compared to the HD MP.



**Figure S21.** Kaplan-Meier Plot of in-hospital survival for admitted COVID-19 patients whose duration on methylprednisolone (MP) was  $\leq 7$  days, between 7 and 14 days and  $> 7$  days. Out of the 247 patients on MP treatment for  $\leq 7$  days the LD MP cohort, 89 (35.0%) expired during COVID-19 hospital stay. Out of the 91 patients on MP treatment between 7 and 14 days, 36 (39.5%) expired during COVID-19 hospital stay. Out of the 41 patients on MP treatment for 14 days, 18 (44.0%) expired during COVID-19 hospital stay. 30-Day and 60-Day In-hospital survival for MP Dose  $\leq 7$  days cohort were 32.2% (95% CI 22.3% to 42.9%) and 29.9% (95% CI 20.0% to 40.9%), respectively. 30-Day and 60-Day In-hospital survival for the MP Dose 7-14 days cohort were 48.1% (95% CI 35.0% to 61.3%) and 38.5% (95% CI 23.4% to 55.0%), respectively. 30-Day and 60-Day In-hospital survival for the MP Dose  $> 14$  days cohort were 71.7% (95% CI 54.9% to 85.9%) and 36.6% (95% CI 16.4% to 59.7%), respectively. The difference in In-hospital survival between the MP Dose  $\leq 7$  days (median=19.0 days (95% CI 17.0 to 23.0 days)] , MP Dose 7-14 days (median =30.0 days (95% CI 19.0 to N/A days)] and MP Dose  $> 14$  days (median =44.0 days (95% CI 32.0 to 60 days)] was statistically significant (Log-rank  $P=0.0011$ ). These data indicate there was survival benefit for the patients that were treated with MP for  $> 14$  days and between 7 and 14 day throughout the Day 60 follow-up compared to patients treated for less than 7 days.



**Figure S22.** Kaplan-Meier Plot of in-hospital survival for admitted COVID-19 patients duration since onset of symptoms to initiation of methylprednisolone (MP) dose that was  $\leq 7$  days, between 7 and 14 days and  $>7$  days. Out of the 181 patients who had MP treatment started within  $\leq 7$  days of onset of symptoms, 86 (47.3%) expired during COVID-19 hospital stay. Out of the 41 patients who had MP treatment started between 7 and 14 days since onset of symptoms, 9 (22.0%) expired during COVID-19 hospital stay. Out of the 153 patients who had MP treatment started after 14 days since onset of symptoms, 48 (31.4%) expired during COVID-19 hospital stay. 30-Day and 60-Day In-hospital survival for the MP dose initiation  $\leq 7$  days since onset of symptoms cohort were 36.8% (95% CI 27.4% to 46.6%) and 14.8% (95% CI 3.8% to 31.1%), respectively. 30-Day and 60-Day In-hospital survival for the MP dose initiation between 7-14 days since onset of symptoms cohort were 41.4% (95% CI 28.9% to 54.6%) and 0, respectively. 30-Day and 60-Day In-hospital survival for the MP dose initiation after 7 days since onset of symptoms cohort were 71.6% (95% CI 53.2% to 86.8%) and 65.1% (95% CI 44.5% to 83.0%), respectively. The difference in In-hospital survival between the symptom duration  $\leq 7$  days (median=20.0 days (95% CI 17.0 to 26.0 days) , symptom duration 7-14 days (median =27.0 days (95% CI 23.0 to 42 days) and symptom duration  $>14$  days N/A was statistically significant (Log-rank  $P=0.0008$ ). These data indicate there was survival benefit for the patients who MP treatment was started  $>14$  days and between 7 and 14 day since the onset of symptoms compared to patients with MP initiation within 7 days of onset of symptoms.





**Table S14.** Need for Supplemental Oxygen versus Methylprednisolone Dose Duration (n=379)

<i>&lt; 7 -Day Duration(n=247)</i>	Methylprednisolone Dose Duration		
	LD MP	HD MP	P-value
Supplemental Oxygen			
None	41 (29.4)	35 (32.4)	
Non-Mechanical Ventilation	49 (35.3)	29 (26.9)	0.3705
Mechanical Ventilation	49 (35.3)	44 (40.7)	
<i>&lt; 7-14 -Day Duration (n=91)</i>			
None	12 (22.6)	10 (26.3)	
Non-Mechanical Ventilation	12 (22.6)	5 (13.2)	0.5212
Mechanical Ventilation	29 (54.7)	23 (60.5)	
<i>&gt; 14 -Day Duration (n=41)</i>			
None	2 (8.7)	2 (11.1)	
Non-Mechanical Ventilation	5 (21.7)	1 (5.6)	0.3241
Mechanical Ventilation	16 (69.6)	15 (83.3)	