




# Body Mass Index, Multi-Morbidity, and COVID-19 Risk Factors as Predictors of Severe COVID-19 Outcomes

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## Abstract

**Purpose:** The purpose of the present study was to investigate body mass index, multi-morbidity, and COVID-19 Risk Score as predictors of severe COVID-19 outcomes. **Patients:** Patients from this study are from a well-characterized patient cohort collected at Mayo Clinic between January 1, 2020 and May 23, 2020; with confirmed COVID-19 diagnosis defined as a positive result on reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assays from nasopharyngeal swab specimens. **Measures:** Demographic and clinical data were extracted from the electronic medical record. The data included: date of birth, gender, ethnicity, race, marital status, medications (active COVID-19 agents), weight and height (from which the Body Mass Index (BMI) was calculated, history of smoking, and comorbid conditions to calculate the Charlson Comorbidity Index (CCI) and the U.S Department of Health and Human Services (DHHS) multi-morbidity score. An additional COVID-19 Risk Score was also included. Outcomes included hospital admission, ICU admission, and death. **Results:** Cox proportional hazards models were used to determine the impact on mortality or hospital admission. Age, sex, and race (white/Latino, white/non-Latino, other, did not disclose) were adjusted for in the model. Patients with higher COVID-19 Risk Scores had a significantly higher likelihood of being at least admitted to the hospital (HR = 1.80; 95% CI = 1.30, 2.50;  $P < .001$ ), or experiencing death or inpatient admission (includes ICU admissions) (HR = 1.20; 95% CI = 1.02, 1.42;  $P = .028$ ). Age was the only statistically significant demographic predictor, but obesity was not a significant predictor of any of the outcomes. **Conclusion:** Age and COVID-19 Risk Scores were significant predictors of severe COVID-19 outcomes. Further work should examine the properties of the COVID-19 Risk Factors Scale.

## Keywords

obesity, BMI, pandemic, Risk Score, COVID-19, comorbidity

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## Introduction

The novel coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has become the worst serious global threat to humanity in the last century. The first case of COVID-19 was reported in China in December 2019<sup>1</sup> and since that time SARS-CoV-2 has spread at a rapid pace through 223 countries, resulting in more than 100 million confirmed cases and over 2 million deaths as of January 29, 2021.<sup>2</sup> The United States (U.S.) has surpassed all countries in number of laboratory-confirmed cases of COVID-19 and associated fatalities with over 25 million infections and 500 000 deaths.

Clinical presentation of patients infected with COVID-19 is highly variable. A spectrum of non-specific signs and symptoms, ranging from asymptomatic infection or flu-like illness, to pneumonia, acute respiratory distress syndrome, and multi-organ failures<sup>3-5</sup> has been described; moreover, concerns have emerged regarding the virus disproportionately impacting

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special populations such as patients with multi-morbidity. The term multi-morbidity refers to the presence of 2 or more long-term conditions (LTCs) that cannot currently be cured but can be controlled through medications or other treatments.<sup>6</sup>

The risk for severe COVID-19 illness (eg, illness requiring hospitalization, intensive care unit [ICU] admission, mechanical ventilation, or resulting in death) seems to increase with the presence of LTCs such as hypertension, diabetes, chronic obstructive pulmonary disease, obesity, cardiovascular diseases, and chronic kidney disease.<sup>7-11</sup> In the U.S. a recent analysis found that hospitalizations were 6 times higher, ICU admissions 5 times higher, and deaths 12 times higher among patients with underlying medical conditions, compared to those without.<sup>12</sup>

Obesity, hypertension, and diabetes are commonly present in higher proportions than other LTCs among COVID-19 patients who had poorer outcomes<sup>13,14</sup>; however, conflicting results have been reported regarding the relation of LTCs and risk of severe COVID-19 illness compared with these comorbidities individually which suggest that a combined effect of these comorbidities may play a key role. A pathophysiological mechanism explaining these associations has not been established; however, many chronic diseases including obesity,<sup>15</sup> share several standard features with infectious disorders—a chronic pro-inflammatory state, and the attenuation of the innate immune response which may make individuals more susceptible to disease complications.<sup>9,16-18</sup>

Clinical characteristics and predictors of severe disease in the U.S. have not been fully defined. Additionally, population differences may limit generalizability of published findings. A better understanding regarding the presence of comorbidities and COVID-19 outcomes can assist with risk stratification at a population level, and allow appropriate management according to target groups who require an individualized assessment and care plan regarding the presence of 1 or multiple comorbidities. The present study sought to examine risks of multi-morbidity and severe COVID-19 outcomes.

## Methods

This study (IRB# 20-002783) was reviewed by The Institutional Review Board (IRB) and determined to be exempt under section 45 CFR 46.101, item 2. During the study, all significant changes to study design and procedures continued to be appropriately filed and reviewed by the IRB which continued exemption determination status.

### Patient Sample

This historical cohort is comprised of consecutive patients (aged 18 years or older) screened (in the presence or absence of symptoms) for COVID-19 at either the Mayo Clinic Rochester or Health System between January 1, 2020 and

May 18, 2020, with a confirmed COVID-19 diagnosis defined as a positive result on reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assays from nasopharyngeal swab specimens (see Table 1).

### Measures

Demographic and clinical data were extracted from the electronic medical record. The data included: date of birth, gender, ethnicity, race, marital status, medications (active COVID-19 agents), weight and height (from which the Body Mass Index (BMI) was calculated, history of smoking, and comorbid conditions (see Table 2) to calculate the Charlson Comorbidity Index (CCI)<sup>19</sup> and the U.S. Department of Health and Human Services (DHHS) multi-morbidity score.<sup>20</sup> Primary study outcome data were also extracted from the patients record and included: admission/discharge dates, ICU admission, and hospital mortality.

Of the 1169 patients initially identified, 1027 patients had anthropometric data available and were included in the BMI analysis. BMI (kg/m<sup>2</sup>) was calculated from height and weight on admission. If admission height and weight were not available, last recorded height and weight were obtained from the patient's record.

The DHHS multi-morbidity score was defined as the cumulative increase burden of 20 conditions proposed by the U.S. Department of Health and Human Services (DHHS).<sup>20,21</sup> International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10) codes were used to define the 20 chronic conditions proposed and data were retrieved electronically from the Rochester Epidemiology Project (REP)<sup>22</sup> within a 5-year capture frame from COVID-19 diagnosis.

The severity weighted CCI was assessed to measure of total comorbidity burden which might predict mortality risk.<sup>19,23</sup> A total of 16 comorbidities are included. The lowest score of 0 corresponds to a 98% estimated 10-year survival rate. Increasing age in decades older than age 50 years and comorbidities increase the total score and decrease the estimated 10-year survival. A score of 7 points and above corresponds to a 0% estimated 10-year survival rate. Coding algorithms for the CCI are detailed elsewhere.<sup>19</sup>

The COVID-19 Risk Score is a Mayo specific modification to an Epic generated COVID score created to assist clinicians with the timely triage and care of patients who tested positive for COVID-19; with the ultimate goal of identifying COVID-19 positive patients who require a higher level of care by being able to triage them timely and appropriately to prevent or mitigate an adverse outcome. Criteria involved in the calculation of the score include presence of hypertension, heart disease, chronic lung conditions including COPD and asthma, chronic liver or kidney disease, diabetes, immune-compromising states, nursing home residency, age, gender (male), and pregnancy. Responses were equally weighted, except age which returns 3 points

**Table 1.** Patient Characteristics.

	Total (N= 1169)
<b>BMI</b>	
Mean (SD)	29.8 (7.28)
Median	28.6
Range	15.5, 66.8
Missing	142
<b>Weight class, n (%)</b>	
Underweight	23 (2.2)
Normal	243 (23.7)
Overweight	334 (32.5)
Obese 1	218 (21.2)
Obese 2	115 (11.2)
Obese 3	94 (9.2)
Missing	142
<b>Gender, n (%)</b>	
Female	593 (50.7)
Male	575 (49.2)
Unknown	1 (0.1)
<b>Race, n (%)</b>	
American Indian/Alaskan Native	6 (0.5)
Asian	68 (5.8)
Black or African American	274 (23.4)
Choose not to disclose	11 (0.9)
Native Hawaii/Pacific Islander	3 (0.3)
White	807 (69.0)
<b>Ethnicity, n (%)</b>	
Choose not to disclose	78 (6.7)
Hispanic or Latino	191 (16.3)
Not Hispanic or Latino	900 (77.0)
<b>Age</b>	
Mean (SD)	43.9 (17.56)
Median	40.6
Range	18.0, 99.0
<b>Marital status, n (%)</b>	
Divorced	57 (4.9)
Life partnership	8 (0.7)
Married	565 (48.4)
Separated	8 (0.7)
Single	471 (40.4)
Unknown	24 (2.1)
Widowed	34 (2.9)
Missing	2
<b>COVID severity scale</b>	
Mean (SD)	1.4 (1.57)
Median	1.0
Range	0.0, 9.0
<b>Charlson Index</b>	
Mean (SD)	0.3 (1.13)
Median	0.0
Range	0.0, 13.0
<b>DHHS multi-morbidity score</b>	
Mean	
Median	1
Range	0.0, 12.0

(continued)

**Table 1. (continued)**

	Total (N= 1169)
<b>Alcohol mod sev, n (%)</b>	
0	1161 (99.3)
1	8 (0.7)
<b>Smoking status, n (%)</b>	
Current	150 (12.8)
Former	174 (14.9)
Never	845 (72.3)
<b>Pregnant at baseline, n (%)</b>	
No	1149 (98.3)
Yes	20 (1.7)

**Table 2.** Comorbidities.

	Total (N= 1169)
<b>Baseline hypertension, n (%)</b>	
No	965 (82.5)
Yes	204 (17.5)
<b>Baseline CAD, n (%)</b>	
No	1110 (95.0)
Yes	59 (5.0)
<b>Baseline arrhythmia, n (%)</b>	
No	1122 (96.0)
Yes	47 (4.0)
<b>Baseline CHF, n (%)</b>	
No	1139 (97.4)
Yes	30 (2.6)
<b>Baseline DLP, n (%)</b>	
No	982 (84.0)
Yes	187 (16.0)
<b>Baseline diabetes, n (%)</b>	
No	1038 (88.8)
Yes	131 (11.2)
<b>Baseline stroke/CVD, n (%)</b>	
No	1152 (98.5)
Yes	17 (1.5)
<b>Baseline asthmatic, n (%)</b>	
No	1081 (92.5)
Yes	88 (7.5)
<b>Baseline COPD, n (%)</b>	
No	1092 (93.4)
Yes	77 (6.6)
<b>Baseline chronic liver disease, n (%)</b>	
No	1125 (96.2)
Yes	44 (3.8)
<b>Baseline CKD, n (%)</b>	
No	1124 (96.2)
Yes	45 (3.8)
<b>Baseline PUD, n (%)</b>	
No	1167 (99.8)
Yes	2 (0.2)

(continued)

**Table 2. (continued)**

	Total (N=1169)
Baseline rheumatoid arthritis, n (%)	
No	1158 (99.1)
Yes	11 (0.9)
Baseline osteoporosis, n (%)	
No	1151 (98.5)
Yes	18 (1.5)
Baseline cancer, n (%)	
No	1109 (94.9)
Yes	60 (5.1)
Baseline HIV, n (%)	
No	1168 (99.9)
Yes	1 (0.1)
Baseline autism, n (%)	
No	1167 (99.8)
Yes	2 (0.2)
Baseline dementia, n (%)	
No	1134 (97.0)
Yes	35 (3.0)
Baseline depression, n (%)	
No	942 (80.6)
Yes	227 (19.4)
Baseline schizophrenia, n (%)	
No	1163 (99.5)
Yes	6 (0.5)
Baseline anxiety, n (%)	
No	953 (81.5)
Yes	216 (18.5)
Baseline SAD, n (%)	
No	1155 (98.8)
Yes	14 (1.2)

for ages 80 and above, 2 points for ages 70 to 79, and 0 for those under 60. Patients were characterized as low (0-2 points), medium (3-5 points), or high risk (6 or more points). The validation of this COVID-19 Risk Score is currently in submission.<sup>24</sup>

## Analyses

Patient characteristics were described using mean, standard deviation, and range for continuous variables and frequencies and percentages for categorical variables. Comorbidities that were present at baseline were reported using percentages. Three separate outcomes were considered: (i) time to mortality or any hospital admission (ie, emergency room, inpatient, or ICU admission) (ii) time to mortality, ICU admission, or inpatient admission (iii) time to mortality or ICU admission. Surveillance occurred from the date of the COVID-19 positive test until last available follow-up or and May 25, 2020. There were 4 main independent variables of interest: BMI, COVID-19 severity scale, Charlson

score, and the DHHS score. For each variable, Cox proportional hazards models were used to determine the impact on mortality or hospital admission. Age, sex, and race (white/Latino, white/non-Latino, other, did not disclose) were adjusted for in the model. Univariate Cox models for each of the adjusted variables were also run. All Cox model results are reported using the hazard ratio, 95% confidence interval, and *P*-value. The proportional hazards assumption was checked for all models using Schoenfeld residual plots for continuous variables and Kaplan-Meier plots for categorical variables. A *P*-value was considered significant if it was less than .05. SAS statistical software (SAS version 9.4; SAS Institute Inc.) was used for all analyses.

## Results

Patient characteristics are reported in Table 1. The average BMI for the population was 29.8, with a majority of people (32.5%) categorized in the overweight weight class. The patients were mainly white (69.0%), female (50.7%), married (48.4%), had never smoked (72.3%), and were an average age of 44 (SD=17.6). Comorbidities of interest were also recorded and are reported in Table 2. Depression (19.4%), Anxiety (18.5%), and Hypertension (17.5%) were the most prevalent conditions reported.

BMI, the COVID-19 Risk Score, the Charlson comorbidity index, and the DHHS score were analyzed independently of each other for the 3 separate outcomes. Correlation between COVID-19 Risk Score with the Charlson comorbidity index, and DHHS score were 0.47 ( $P < .001$ ) and 0.73 ( $P < .001$ ), respectively. Charlson comorbidity index and DHHS score correlated by 0.59 ( $P < .001$ ). The outcome of time to death or any hospitalization (Admission, Inpatient, or ICU) is shown in Table 3. Of the 1027 patients with available anthropometric data, 20.4% (N=209) were admitted and 2.1% (N=22) died. A total of 7.1% (N=73) were admitted to inpatient services while 1.6% (N=16) required ICU admissions. After adjusting for age, sex, and race those with a higher COVID-19 Risk Score had a significantly higher likelihood of being at least admitted to the hospital (HR=1.80; 95% CI=1.30, 2.50;  $P < .001$ ).

The results from the Cox models with an outcome of death or inpatient admission (includes ICU admissions) are reported in Table 4. Unadjusted hazard ratios are reported for all variables that are analyzed in the adjusted models. After adjusting for age, sex, and race the COVID-19 risk score predicted a significantly higher likelihood of having worse outcomes for each 1 unit increase in the score (HR=1.20; 95% CI=1.02, 1.42;  $P = .028$ ).

Table 5 shows the results for the Cox models with the outcome of time to either mortality or ICU admission. After adjusting for age, sex, and race BMI, COVID-19 risk score, Charlson index score, and DHHS score did not significantly impact the likelihood of death or ICU admission.

**Table 3.** Cox Model for Time to Mortality or Any Admission (ie, Emergency Room, Inpatient, or ICU Admission).

	Unadjusted hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
BMI (unit=5)	1.03 (0.94, 1.13)	.551	1.02 (0.93, 1.12)*	.724
COVID-19 severity scale (unit=3)	2.02 (1.68, 2.43)	<.001	1.80 (1.30, 2.50)*	<.001
Charlson score (unit=1)	1.11 (1.03, 1.20)	.010	1.00 (0.91, 1.09)*	.953
DHHS score (unit=1)	1.14 (1.08, 1.20)	<.001	1.03 (0.96, 1.11)*	.407
Female vs male	0.99 (0.76, 1.29)	.945		
Age (unit=1)	1.02 (1.02, 1.03)	<.001		
White/Latino vs White/Non-Latino	1.20 (0.84, 1.71)	.325		
Other vs White/Non-Latino	1.07 (0.78, 1.46)	.669		
Chose not to disclose vs White/Non-Latino	0.52 (0.17, 1.65)	.268		

\*Separate models for each variable that adjusts for age, sex, and race (white/Latino, white/non-Latino, other, did not disclose).

**Table 4.** Cox Model for Time to (ii) Time to Mortality, ICU Admission, or Inpatient Admission.

	Unadjusted hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
BMI (unit=5)	1.03 (0.89, 1.19)	.685	1.10 (0.94, 1.28)*	.235
COVID-19 severity scale (unit=1)	1.58 (1.45, 1.72)	<.001	1.20 (1.02, 1.42)*	.028
Charlson score (unit=1)	1.21 (1.10, 1.32)	<.001	0.98 (0.87, 1.11)*	.787
DHHS score (unit=1)	1.24 (1.15, 1.34)	<.001	0.98 (0.88, 1.08)*	.681
Female vs male	0.65 (0.42, 1.00)	.051		
Age (unit=1)	1.06 (1.05, 1.07)	<.001		
White/Latino vs White/Non-Latino	0.83 (0.44, 1.54)	.550		
Other vs White/Non-Latino	0.68 (0.39, 1.18)	.170		
Chose not to disclose vs White/Non-Latino	0.42 (0.06, 3.02)	.387		

\*Separate models for each variable that adjusts for age, sex, and race (white/Latino, white/non-Latino, other, did not disclose).

**Table 5.** Cox Model for Time to Time to Mortality or ICU Admission.

	Unadjusted hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
BMI (unit=5)	0.93 (0.73, 1.19)	.583	1.03 (0.79, 1.34)*	.846
COVID-19 severity scale (unit=1)	1.64 (1.45, 1.87)	<.001	1.09 (0.85, 1.40)*	.512
Charlson score (unit=1)	1.25 (1.10, 1.43)	.001	0.99 (0.83, 1.18)*	.893
DHHS score (unit=1)	1.21 (1.07, 1.36)	.002	0.88 (0.75, 1.03)*	.110

\*Separate models for each variable that adjusts for age, sex, and race (white/Latino, white/non-Latino, other, did not disclose).

## Discussion

The results of this study show a remarkably consistent pattern. Across all 3 outcomes types, in unadjusted models, higher multi-morbidity and higher COVID-19 risk scores translate to higher risk of severe COVID-19 outcomes. Obesity does not have the same effect. However, once multi-morbidity and COVID-19 risk scores were adjusted for the effects of demographic variables, a consistent pattern emerged. Age was the only significant demographic

predictor of severe COVID-19 outcomes, and this accounted for the effects of multi-morbidity but not COVID-19 risk scores which remained significant predictors of severe COVID-19 outcomes. This indicates that, in addition to age, other components of the COVID-19 risk score provide important information for predicting outcomes. This pattern was consistent across all 3 outcomes.

The finding in the present study showing that obesity was not associated with severe COVID-19 outcomes is not consistent with conclusions from other reviews of studies on

obesity and COVID-19 outcomes.<sup>25,26</sup> However, many of the studies included in these reviews have used much smaller samples than in the present study. One larger study (N=5700) simply reported obesity as a comorbidity in COVID-19 positive patients, but did not examine it as a risk factor per se.<sup>4</sup> Another review of 6 studies including over 26000 patients examining obesity as a risk factor for COVID-related mortality showed that patients with BMI > 25 had 3.68 times greater risk of mortality.<sup>27</sup> However, there was significant variation in the results across studies with 2 smaller studies with N=48 and 224 showing odds ratios of 49 and 38, respectively. The largest study showed an odds ratio of 1.55. Perhaps there is a possibility that some of the studies on obesity and COVID-19 outcomes suffer from small sample bias. That said, it remains possible that obesity could predict heightened risk for severe COVID-19 outcomes even though it was not a predictor in any unadjusted or adjusted analyses in the present manuscript. Indeed, many proposed mechanisms for action have been proposed and will likely continue to be investigated.<sup>28</sup>

Finding that multi-morbidity scores in the present study were associated, in unadjusted analyses, with increased risk of severe outcomes of COVID-19 is consistent with some existing literature. For instance, a large (N=1591) study of Italian COVID-19 patients showed that survivors had lower CCI scores than nonsurvivors.<sup>29</sup> In a small Indian study of 206 deceased patients, it was determined that over 50% had pre-existing comorbidities.<sup>30</sup> And, in a meta-analysis of 5 studies examining multimorbidity and COVID-19-related mortality, the pooled odds ratio was 1.8 suggesting that in over 4000 patients those with a higher degree of multimorbidity were at increased risk of death.<sup>27</sup> Given the higher risk of individuals with multimorbidity, it is also important to consider that 2 very large studies from the United Kingdom utilizing the UK Biobank Cohort suggest that multi-morbidity, in addition to raising the risk of adverse outcomes, also raises the risk of initial COVID-19 infection as well. In 1 study investigators compared COVID-19 positive patients to patients who were COVID-19 negative and not-tested patients. In this analysis of 428 199 patients, of which 1324 tested positive for COVID-19, patients with 2 or more comorbidities showed greater risk of testing positive for COVID-19.<sup>31</sup> But in a separate study of 502 640 patients, of which 1326 tested positive, with comparisons between patients who tested positive, patients who tested negative, and not-test patients, multimorbidity predicted greater risk of testing positive, but only when compared to not-tested patients.<sup>32</sup> Differences between COVID-19 positive and COVID-19 negative patients in levels of multimorbidity were not statistically significant. In summary, the current results confirm existing work from multiple regions of the world showing the multimorbidity raises the risk of severe COVID-19 outcomes.<sup>33</sup> However, it is important to note that when the present findings were adjusted for the effects of demographic variables, the association between multi-morbidity and severe COVID-19 outcomes was

completely accounted for and age was the only statistically significant demographic predictor.<sup>34</sup>

The present study included an unvalidated clinical risk assessment measure, the COVID-19 Risk Score.<sup>24</sup> This assessment is unique and was intended only for use with COVID-19 patients making it quite unlike the CCI or DHHS comorbidity measures. The COVID-19 Risk score includes risk factors from a variety of socio-demographics (eg, age, residence), medical conditions, (eg, hypertension, COPD, diabetes), and symptoms (eg, dyspnea, chest pain) that are specifically understood to increase risk of poorer COVID-19 outcomes. That is, the COVID-19 Risk Score is far more specific to COVID-19, unlike other more general comorbidity indices. The COVID-19 Risk Score was the only measure to predict severe COVID-19 outcomes in models that adjusted for baseline demographic factors.<sup>34</sup> In this context, Wongvibulsin et al<sup>34</sup> recently reported favorable results on the utility of readily available clinical information as an accurate tool to predict COVID-19 progression to severe illness or death. Underscoring the clinical utility of demographic variables demographic, medical, and symptom in the prediction of disease progression.

Perhaps the most consistent and robust effect in our analyses, and one that accounted for the effects of comorbidities but not COVID Risk Score, was a patient's age. This is consistent with results of a UK Biobank sample of 470 034 individuals in which individuals 75 years of age or older had higher risk of mortality (OR=13) compared to individuals less than 65 years of age.<sup>35</sup> Similarly, in a sample of 548 patients with COVID-19 in Wuhan, China, patients aged 65 years or older had a 1.7 times greater risk of mortality.<sup>36</sup> A meta-analysis of 6 studies including about 46000 individuals confirmed that individuals over the age of 70 were at 6 times greater risk of mortality than individual less than 70 years.<sup>27</sup> Age appears a consistent and robust predictor of severe COVID-19 outcomes.

This study does have several inherent limitations. The sample has some diversity but is reflective of the population from which it is drawn which is upper-midwestern, largely monoethnic, and rural. Therefore, our findings have limited generalizability. The cohort used includes patient data collected during the early months of the COVID-19 pandemic when COVID specific therapeutics were not available. Therefore, our results may not reflect the impact of the pandemic in later phases. Patients in this sample are from a single medical site. Finally, key predictor in this study (COVID-19-Risk Score) was an unvalidated measure, although this is currently in progress and the manuscript detailing the development of this score and validation method is in submission.

## Conclusion

The present study offers some intriguing insights on risk factors for severe COVID-19 outcomes. Perhaps the clearest emerging risk factor identified in the present

and previous studies is older age. Multimorbidity is an important risk factor to consider as it appears in other studies to contribute to risk of infection and in the present and other studies to risk of severe outcomes, but evidence of the latter association is much less developed. Present findings suggest that multimorbidity may be related to increased risk of severe COVID-19 outcomes but this is explained by older age in the present analyses. This is an important area for future consideration. The question remains: Is multimorbidity simply a proxy for older age or are there distinct effects in the setting of COVID-19? COVID-19 risk factors as assessed by the COVID-19 Risk Score appear to be the strongest predictor of severe COVID-19 outcomes, even after controlling for demographic factors. The COVID-19 Risk Score is unvalidated, yet an important predictor of risk. Consequently, future work should carefully examine the survey, refine the items on the assessment, consider any relevant training necessary for physicians to administer the survey, and potentially develop patient-completed versions. Work is currently underway to develop psychometrics including reliability, validity, sensitivity/specificity, and improve ease and standardization of administration. These improvements will allow for greater use and deployment in predicting what patients might be at most risk of severe outcomes. With valid and easy-to-use tools such as the COVID-19 Risk Score, better care and treatment might more readily be made available to patients who are in most need and in this way providers can serve patients in more effective ways during this pandemic.

### Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: All authors declare no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; and no other relationships or activities that could appear to have influenced the submitted work. RTH reports consulting fees from Nestlé, and research funding from an IIR grant with Zealand Pharmaceuticals.

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### Ethics and Consent to Participate

In accordance with the Declaration of Helsinki, this study was reviewed and approved (ID 20-002783) by the Mayo Clinic Institutional Review Board (IRB). Mayo Clinic IRB approved informed consent waiver.

### Ethical Standards

This study was determined to be EXEMPT under 45 CFR 46.101, Item 2 by the Mayo Clinic Institutional Review Board which had

ethical oversight for this study. In addition, the authors assert that all procedures contributing to this work comply with the ethical standards of the Mayo Clinic Institutional Review Board guidelines on human experimentation in accordance with the Declaration of Helsinki of 1975, as revised in 2008.

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### Availability of Data and Materials

All data supporting the study findings are contained within this manuscript.

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