EVIDENCE SUMMARY

Among adult patients diagnosed with COVID-19, should prognostic models be used to predict the likelihood of severe disease and mortality?

Updated by: Bryan F. Elvambuena, MD, Michelle Cristine Miranda, MD & Howell Henrian G. Bayona, MSc
Initial Review by: Patricia Pauline Remalante-Rayco, MD, Evelyn Salido, MD, MSc and Maria Teresa S. Tolosa, MD, D Clin Epi, FPDS

RECOMMENDATIONS

<u>To guide the decision to admit adult patients with COVID-19 to the hospital:</u>
We suggest the use of age, BUN, number of comorbidities, CRP, SpO2/FiO2 ratio, platelet count, Heart rate (ABC2-SPH) risk score, Confusion Urea Respiration Blood Pressure (CURB-65) severity score, Risk Stratification in the Emergency Department in Acutely Ill Older Patients (RISE-UP) score, and Rapid Emergency Medicine Score (REMS). *(Low certainty of evidence; Weak recommendation)*

There is insufficient evidence to recommend the use of 4C Mortality Score, COVID Outcome Prediction in the Emergency Department (COPE) model, and Quick Sepsis-related Organ Failure Assessment (qSOFA) score. *(Very low certainty of evidence)*

<u>To guide in the expectant monitoring of hospitalized adult patients:</u>
We suggest the use of the 4C Deterioration model. *(Low certainty of evidence; [Weak] recommendation)*

There is insufficient evidence to recommend the use of Modified Early Warning Score (MEWS) and National Early Warning Score 2 (NEWS2), Clinical Frailty Scale (CFS), and the COVID-GRAM model. *(Very low certainty of evidence)*

Consensus Issues
The recommendations on prognostic models are limited to adult patients since the evidence base included studies only on the adult population. No studies were conducted among pediatric patients. The panelists were unanimous in all recommendations on prognostic models.

PREVIOUS RECOMMENDATIONS

<u>To guide the decision to admit patients with COVID-19 to the hospital:</u>
We suggest the use of Age, BUN, number of Comorbidities, CRP, SpO2/FiO2 ratio, Platelet count, Heart rate (ABC2-SPH) risk score, Confusion Urea Respiration Blood Pressure (CURB-

65) severity score, Risk Stratification in the Emergency Department in Acutely Ill Older Patients (RISE-UP) score, and Rapid Emergency Medicine Score (REMS). *(Low quality of evidence; Conditional recommendation)*

There is insufficient evidence to recommend the use of 4C Mortality Score, COVID Outcome Prediction in the Emergency Department (COPE) model, and Quick Sepsis-related Organ Failure Assessment (qSOFA) score*. (Very low quality of evidence)*

To guide in the expectant monitoring of hospitalized patients:
We suggest the use of the 4C Deterioration model. *(Low quality of evidence; Conditional recommendation)*

There is insufficient evidence to recommend the use of Modified Early Warning Score (MEWS) and National Early Warning Score 2 (NEWS2). *(Very low quality of evidence)*

Consensus Issues
There was a high certainty of evidence that the QCOVID model can predict mortality from COVID-19. However, there was an issue on applicability as some of the components of this model (i.e., geographic region and Townsend deprivation quintile) is specific for the general population of England. Hence, its use warrants reconsideration of the component prognostic factors and validation in the Philippine setting before any recommendations can be made.

It was noted that the qSOFA model was already being used by some hospitals and centers in the Philippines. Clinicians should be guided on its use as it was found to have a very low quality of evidence for prediction of mortality of inpatients. There are other prognostic models such as the CURB-65, RISE-UP and REMS which are pre-existing models designed for specific patient populations and the ABC2-SPH model which has a good discrimination performance. All of these were found to have better quality of evidence compared with qSOFA. The 4C Mortality score and COPE model were also found to have a very low quality of evidence to predict mortality. Further, it was observed that there was a decrease in the discriminatory ability of the COPE model when externally validated. In terms of clinical deterioration, the 4C deterioration score was found to have a better predictive ability and

What's new in this version?

- New validation studies for COVID-GRAM and Clinical Frailty Scale were added.
- Two other studies on 4C Mortality Score were added.

Key Findings

- In this version, two new prognostic models were reviewed and 13 new studies were added. One study is a binational prospective cohort which validated 4C mortality score and COVID-GRAM on a larger population in South America and Europe. Three more studies validated COVID-GRAM but have an overall unclear risk of bias and low quality of evidence. Nine studies validated the use of Clinical Frailty Scale in prognosticating elderly COVID-19 patients, but the overall assessment for risk of bias was rated high and the level of evidence was rated very low.
- In total, 46 cohort studies on prognostic models for clinical deterioration and mortality of individuals with COVID-19 were found. Most of the studies (n=36) were assessed to have high risk of bias due to issues in participant selection and analysis. There were eight studies with unclear, and two with low risk of bias.

- For predicting mortality, the following models demonstrated fair-to-good predictive ability: 4C mortality score, ABC2-SPH, CURB-65, REMS, RISE UP and COVID-GRAM models. Poor to fair prediction was noted for the qSOFA model, with one new study yielding lower AUC estimates compared to the previously included studies. Only one model, the QCOVID model for mortality validated for the UK setting, demonstrated high predictive ability.
- For predicting clinical deterioration, available prognostic models showed varied performance. The 4C deterioration which has been investigated in only one study with low risk of bias, showed fair predictive ability. The MEWS model has poor prediction of clinical deterioration while NEWS2 has inconsistent prediction (poor to good). The Clinical Frailty Scale (CFS), increases the risk of mortality among elderly COVID-19 patients.
- None of these models has been validated in the Philippine population. Thus, validation studies are needed before these models can be used to inform practice.

Introduction

As of December 06, 2021, there have been a total of 265,194,191 confirmed cases of COVID-19 reported to WHO. In the Philippines, deaths have numbered to 49,591 out of the 2,835,345 cases as of December 7, 2021, 0.1% of which are tagged as severe and critical. In order to reduce the risk of severe disease and mortality, numerous studies have assessed the usefulness of prognostic models that aim to identify patients at high risk of adverse outcomes from COVID-19. These models include early warning scores that were originally developed to identify and monitor inpatients at risk of deterioration (in order to facilitate transfer to intensive care units), or new models that were developed for the purpose of predicting the likelihood of severity or mortality among COVID-19 patients (referred in this report as “pre-existing models” and “COVID-19-specific models”, respectively).

Review Methods

In this version, we extended the literature search to cover for studies published between March 8, 2021 until November 27, 2021 in the following electronic databases: MEDLINE, Cochrane Central, McMaster Evidence Based Alerts, Cornell Open Access Publication (COAP), and Living Overview of the Evidence (L•OVE). Included articles were also hand-searched for their references to supplement yield. Search terms “death” or “mortality”, “severe”, and “predict” were used. The search yielded both published articles and preprints.

The criteria for inclusion of studies were as follows: (1) population: adults diagnosed with COVID-19 infection, (2) intervention: prognostic models with external validation, (3) outcome: worsening severity or clinical deterioration or poor outcomes and/or mortality; and (4) cross-sectional, case-control, or cohort studies. Studies were excluded if they met any of the following criteria: (1) development of prediction models through machine-learning algorithms or artificial intelligence without an available online tool; (2) number of outcome events (severe disease or mortality) <100. There were 45 articles that met our inclusion criteria.

We used the CHecklist for Critical Appraisal and data extraction for Systematic Reviews of prediction Modelling Studies (CHARMS) to plan the review.[5] The Prediction model Risk Of Bias ASsessment Tool (PROBAST) was used as a guide to appraise the risk of bias and concern for applicability for each article as low, high, or unclear.[6] We extracted the following details of the studies: participants, setting, study design, the predictive performance of each model, and methods of calibration and discrimination. Discrepancies in appraisal and data extraction were resolved through discussion and eventual agreement between the two authors.

Results

Characteristics of included studies

As of November 27, 2021, we found 46 studies that met the inclusion criteria.[9-41] Thirteen (13) new studies were added to the 33 studies included in the previous review version. The characteristics of these studies are summarized in Appendix 2.

Setting, Study Design

Most of the studies were done in Europe, specifically in the United Kingdom (16 studies), Spain (6), Netherlands (3), Italy (3), Switzerland (2), Denmark (1), France (1), Belgium (1), Germany (1). The rest were done in the US (6), Mexico (1), Brazil (3), China (4), and Turkey (2). All selected studies were cohorts – eight prospective and 38 retrospective. Most studies were done during the early part of the pandemic (first half of 2020) but ten studies collected data extending to or exclusively during the second half of 2020 up to January 2021. These latter studies may reflect the possible effects of the changing incidence and prevalence of infection on model performance.[7,8]

Population

Most studies obtained data from electronic medical databases of secondary or tertiary medical centers, wherein the prognostic model was applied during the emergency department visit or hospital admission. In seven articles, the data were obtained from cohorts of patients (both ambulatory and hospitalized) whose primary care physicians' electronic health records were linked with hospital data and enrolled in regional, national, or international databases, most of them established even prior to the pandemic. Seven articles involved elderly population, most of which were admitted at ICUs of different hospitals. Most of the studies included confirmed PCR-positive adults with community-acquired COVID. Eight studies included suspected or clinically-diagnosed COVID (typical symptoms, chest CT infiltrates, and the absence of an alternative diagnosis). Three studies specified the inclusion of nosocomial COVID in their population.

Outcomes

The prediction outcome of interest is death in 34 studies, admission to the intensive care unit in seven, or a composite of death or clinical deterioration in twelve studies, and some studies determining multiple outcomes. Another study looked at the survival status of patients after 90 days. Death was determined either during the in-hospital stay or over a specified period of time (14, 28, or 30-day). Clinical deterioration or progression of COVID-19 severity was usually defined as admission to an intensive care setting, need for oxygen supplementation (non-invasive or mechanical ventilation), or death. One study looked at thromboembolism as an outcome. Among the studies done in the general population, the mortality rate was 0.020 to 0.077% in the England population and 8.2% in the Denmark population. The mortality rate among hospitalized patients was 5.5 to 45.63%.

Exposure

Twenty-two studies validated 14 different pre-existing prediction models (pre-COVID-19 pandemic). Twenty-three articles focused on the development and/or validation of 44 new models for prediction of outcomes in COVID-19 patients. One study included both pre-existing and COVID-specific models. seven studies validated the use of clinical frailty scale in the prognosis of elderly COVID-19 patients. The components of the models were of varying complexity – from a few patient characteristics to combinations of demographic features, comorbidity, clinical features, and laboratory tests and scales.

Overall summary of methodological quality
The assessments of the 45 articles are presented in Appendix 3.

The overall risk of bias was assessed to be high in 36 (78%) studies, low in two studies, and unclear in eight studies. Contributory to this assessment is the high risk of bias for the participant domain in 11 studies, predictor domain in two studies, outcome domain in six studies and the analysis domain in 23 studies. Particularly for the participant domain, high risk of bias was due to inclusion of severely ill patients that was a result of the studies being done in tertiary centers and specialized COVID-designated hospitals. Some studies excluded patients with incomplete data.

For the analysis domain, causes for high risk of bias include the following: small number of participants with the outcome relative to the number of predictors; mishandling of continuous predictors; exclusion of patients lost to follow up and those with missing data from the analysis; lack of imputation for missing data; selection of predictors based on univariable analysis (leading to loss of information and consequent reduction of the model's predictive ability); lack of accounting for censoring and competing risks, as well as for model overfitting or optimism; and lack of information on model performance measures (usually on calibration).

Among the issues in the predictor and outcome domains are lack of blinding for outcome during data abstraction; lack of clear information on timing of determination of predictors; and insufficient time interval between assessment of predictor and outcome.

Overall concern for applicability was unclear for all studies due to the inclusion of laboratory and/or imaging predictors, which may not be available in many local health facilities. Moreover, a delay in test results due to prolonged laboratory and imaging turnaround time may limit the application of prognostic models that are intended for immediate use to aid patient diagnosis or on admission at the emergency department. Models that include comorbidities as predictors with reliance on ICD-10 may be difficult to apply in our setting because most hospitals lack a readily-available database of comorbidities, leading to potential recall bias.

The GRADEpro Guidance Development Tool (GDT) was used to assess the certainty of evidence for eight models that had multiple validation studies and six models with only one published validation study but had very low to low certainty of evidence (See Appendix 4 for GRADE Evidence Profiles).

Summary of results of included studies
Models with more than one external validation study were focused on in this review to obtain information both about accuracy of the model in predicting the outcome of interest and consistency of prediction (See Table 1). Studies on prognostic models with only one external validation but were assessed to have unclear or low risk of bias are briefly mentioned. In all studies, the ability of a prediction model to discriminate among individuals who will develop an event or outcome (e.g., mortality or severity) from those who will not is measured by the area under the curve (AUC).

Models for prediction of mortality in the general population (ambulatory and hospitalized)
QCOVID model
The QCOVID model developed by Clift et al., [9] and further validated by Nafilyan et al.[10] used data from a large network of primary care datasets with linkage to hospitalization data. It shows excellent discrimination of mortality risk but its use is quite specific to England by the nature of its components (geography, accommodation, Townsend deprivation index) and scoring system. It

has the potential to help patients and doctors reach a shared understanding of mortality risk of COVID-19 diagnosed in the community even prior to the availability of laboratory tests. It was designed to be applied across the adult population for risk stratification for public health purposes during the pandemic, to support shared management of risk and occupational exposure, and in early targeting of vaccines to people most at risk.[9]

The studies of Clift and Nafilyan were assessed to have low risk of bias and high certainty of evidence. However, for the QCOVID model to be used in the Philippines, it has to be modified and validated.

COPE model

The COPE model was also developed from the general population (around 2 million Dutch recruited at the point of RT-PCR testing). Its base model (age, sex, BMI) has excellent prediction of death at point of diagnosis (AUC 0.902) which falls to fair prediction at hospital admission (AUC 0.785). When validated in a UK cohort, prediction of death on diagnosis is much lower (AUC 0.742). This study has unclear risk of bias and the certainty of evidence is low.

Models for prediction of poor outcomes among hospitalized patients

Mortality

CURB-65, REMS, RISE-UP

Pre-existing models such as CURB-65, REMS, and RISE-UP are established scoring systems that were designed for specific patient populations. CURB-65 is a tool that has been validated for use among patients with community-acquired pneumonia for the prediction of 30-day mortality. REMS was intended to predict in-hospital mortality for patients presenting at the emergency department regardless of disease, while RISE-UP was designed for mortality prediction specifically for elderly patients in the emergency room. Several studies have validated these models for use in COVID-19 as most of the affected patients, especially in the early part of the pandemic, were older than 65 years and presented with pneumonia. Their relative simplicity and popular use among clinicians have made them attractive models for risk stratification in COVID-19. These three models were found to have fair to good discriminative performance for mortality when validated in COVID-19 patients, with estimated AUCs ranging from 0.70 to 0.84. However, most validation studies were found to have high risk of bias, with low certainty of evidence, except the one by Gupta et al. (2021), which has unclear risk of bias.

4C Mortality Score

Two studies on prognostic models for mortality among hospitalized patients at low risk of bias deserve some mention. The 4C Mortality Score was developed and validated from the International Severe Acute Respiratory and Emerging Infections Consortium Coronavirus Clinical Characterisation Consortium (ISARIC4C) study, which involved 260 hospitals in the United Kingdom.[12] The model's components (age, sex, number of comorbidities, vital signs and BUN and CRP) are available in most hospitals. The model, which exhibited fair discriminative ability, was developed using a cohort of seriously-ill patients and may not be generalizable to patients in the community with lower mortality risk.

Two new validation studies on 4C Mortality score were reviewed. One is a bi-national study involving the Latin American and Spanish population, however, has fair discrimination (AUC 0.78). The other study involved the Turkish population but also showed fair discrimination (AUC 0.784). Both studies also have low certainty of evidence.

ABC2-SPH

The ABC-SPH model was developed and validated in Brazil using variables commonly available in most emergency departments around the globe (age, number of comorbidity, heart rate, SpO2/FiO2 ratio, BUN, CRP and platelet count).[13] It has an AUC above 0.8, indicating good discrimination. On external validation on a Spanish cohort with patients from the early part of the pandemic, the model was found to potentially underestimate mortality in patients who are at higher risk of death. The certainty of evidence from this study is low.

Other prognostic models

The rest of the models for prediction of mortality among hospitalized patients were at high risk of bias and with very low certainty of evidence.

Clinical Deterioration

4C Mortality Score

A study of 66,136 adults with confirmed COVID-19 belonging to the ISARIC 4C cohort in the UK done by Gupta et al found that most in-hospital deterioration occurred around 4 days (1-9 days) from admission and declined with increasing time thereafter.[14] In-hospital clinical deterioration was defined as a need for non-invasive or invasive oxygen supplementation, admission to an intensive care unit, or death.

Early warning scores (NEWS2, MEWS)

Early warning scores like NEWS2 and MEWS which use easy-to-obtain physical examination findings as predictors for in-hospital deterioration is desired during this early phase of hospitalization. They can easily be used in all clinical settings without need for additional training of medical staff and pose no socio economic issues like cost and availability of tests. However, validation studies of these two prognostic models for clinical deterioration showed poor to fair and poor discrimination indices of NEWS2 and MEWS, respectively.

The study by Gupta mentioned above was found to be of low risk of bias and will be mentioned here briefly. It developed and validated the 4C model for clinical deterioration, for use on admission for community-acquired COVID-19 cases, or at the initial assessment of suspected nosocomial COVID-19. It showed fair discrimination (AUC 0.77; 0.76, 0.78). The certainty of evidence from this study is low.

COVID-GRAM

Four studies provided data on the ability of COVID-GRAM to predict critical illness, 30-day mortality, or ICU requirement among inpatients with COVID-19. The model includes the following as predictors: X-ray abnormality, age, hemoptysis, dyspnea, sensorium, number of comorbidities, cancer history, neutrophil-lymphocyte ratio (NLR), lactate dehydrogenase, and direct bilirubin.

COVID-GRAM was reported to have fair predictive ability for mortality (AUC 0.88 (Armiñanzas), 0.77 (Neto). In studies that reported poor outcome as a composite score, COVID-GRAM was reported to have good predictive ability with an AUC of 0.88 (0.85, 0.91; Liang) and 0.77 (Armiñanzas). However, the majority of the studies did not account for patients with missing data, hence a very serious risk of bias and low certainty of evidence. Moreover, COVID-GRAM has not been validated locally.

Clinical Frailty Scale

The Clinical Frailty Scale is a well-validated scale used to quantify the degree of disability from frailty. Several studies have tried validating its use in the prognosis of elderly COVID-19 patients,

however, only nine studies met the inclusion criteria for this review. The COVIP study assessed the overall survival at 30 days and correlated it with the level of frailty on admission and found out that only 41% of frail COVID patients survived ($p<0.001$). However, this study had a high risk of bias and the overall quality of evidence for the rest of the studies is very low. No AUC values were reported across the studies.

Other prognostic models

The rest of the studies on prognostic models for clinical deterioration of hospitalized patients with COVID-19 were at high risk of bias and with very low certainty of evidence.

Recommendations from Other Groups

The Australian guidelines for the clinical care of people with COVID-19 [42] recommend monitoring of markers of clinical progression, such as rapidly progressive respiratory failure and sepsis, especially on days five to ten after onset of symptoms. This was not developed with an evidence-based framework, but formed through a consensus process.

The WHO COVID-19 Clinical management Living guidance (23 November 2021) [43] recommends the use of clinical judgment, including consideration of patients' values and preferences and local and national policy if available, to guide management decisions including admission to hospital and to the ICU rather than currently available prediction models for prognosis when caring for patients with COVID-19 of any severity assessed in a clinic or hospital (conditional recommendation, very low certainty).

Research Gaps

There are at least one ongoing study registered in clinicaltrials.gov for prediction models for COVID-19 in various countries – one retrospective (case-only) study in China. the CODED study in Italy has already been completed but not yet published.[44-47] These models look at combinations of demographic, clinical, biologic, and/or imaging parameters with or without use of machine-based learning.

Despite the large number of studies being produced, the majority of prediction models for adverse COVID-19 outcomes continue to suffer from selection bias, overfitting, and/or the lack of external validation. Article appraisals and the conduct of systematic reviews have paved the way for improved quality of studies.

Validation of these prognostic models in the Filipino population is needed, and the use of these models must not replace clinical judgment with due consideration of patients' values and preferences. As the predictive performance of a model may differ depending on the setting and population to which it is applied, the importance of conducting external validation studies in settings where the model is intended to be used cannot be overemphasized. Pooling of multicenter data across heterogeneous settings and populations may help increase the robustness of model performance evaluation, especially when substantiated by meta-analyses. Moreover, the studies that met our criteria did not include validation of prognostic models in the pediatric population. With the rising trend in pediatric COVID cases, it is prudent to look in these validation studies as well.

Table 1. Models with more than one external validation study in this review. Prognostic models that have additional studies in this update are highlighted in yellow and in bold.

Model First Author Country	Population	Outcome	Predictors	Risk based on cut-off scores	Discrimination Performance (AUC, 95% CI if provided)*	Online risk calculator
QCOVID Clift [9] Nafilyan [10] (England)	General population	Mortality	Age Sex Geographic region Ethnicity Townsend deprivation quintile Accommodation Body mass index Chronic kidney disease (CKD) Learning disability Chemotherapy Cancer/immunosuppressio nother comorbidities	Online calculator gives absolute risk	Clift Period 1 (Jan-Apr 2020) • Men 0.93 (0.92, 0.93) • Women 0.93 (0.92, 0.94) Period 2 (May-Jun 2020) • Men 0.93 (0.92, 0.95) • Women 0.95 (0.94, 0.96) Nafilyan Period 1 • Men 0.935 (0.933, 0.937) • Women 0.945 (0.943, 0.947) Period 2 • Men 0.944 (0.942, 0.946) • Women 0.956 (0.954, 0.958)	https://qcovid.org
4C Mortality Score Knight [12] (UK) Van Dam [39] (Netherlands) **Neto (Brazil, Spain)** **Doganay (Turkey)**	Inpatients	Mortality (30-day) in-hospital mortality In-hospital mortality ICU requirement	Age Sex Number of comorbidities Respiratory rat Peripheral oxygen saturation Glasgow coma scale (GCS) Blood urea nitrogen (BUN) C-reactive protein (CRP)	Mortality risk (Score range: 0-21) Low: 0-3 Intermediate:4-8 High: 9-14 Very high:≥15	Knight 0.767 (0.76, 0.77) Van Dam 0.84 (0.79, 0.88) **Neto 0.78 (0.75, 0.81)** **Doganay** • **In-hospital mortality 0.784 (0.774, 0.820)** • **ICU requirement 0.797 (0.758, 0.32)**	https://isaric4c.net/risk
Confusion Urea Respiration Blood Pressure (CURB-65) Artero [17] (Spain) Bradley [21] (UK) Liu FY [30] (China) Nava [33] (US) van Dam [39] (Netherlands) **Neto (Brazil,**	Inpatients	Mortality (30-day) Overall mortality	Age Confusion Respiratory rate (RR) Blood pressure BUN		Artero 0.82 (0.82,0.84) Bradley 0.75 Liu FY 0.77 (0.72, 0.81) Nava 0.78 van Dam 0.75 (0.70, 0.80) **Neto 0.74 (0.72,0.77)** **Doganay 0.846 (0.810,0.877)** **Armiñanzas 0.727**	https://www.mdcalc.com/curb-65-score-pneumonia-severity

Spain) Doganay (Turkey) Armiñanzas (Spain)						
Rapid Emergency Medicine Score (REMS) Gupta [27] (UK) Liu FY [30] (China) van Dam [39] (Netherlands	Patients at Emergency Department (ED)	Mortality (in-hospital)	Age Pulse rate (PR Mean arterial pressure (MAP) RR GCS Oxygen saturation (SpO2)		Gupta 0.76 (0.71, 0.81) Liu FY 0.84 (0.8, 0.88) van Dam 0.73 (0.68, 0.78)	https://www.mdcalc.com/rapid-emergency-medicine-score-rems
Risk Stratification in the Emergency Department in Acutely Ill Older Patients (RISE UP) Van Dam [39] Van Dam [40] (Netherlands)	Patients at ED, Inpatients	30-day mortality	Age HR MAP RR SpO2 GCS BUN Bilirubin Albumin Lactate dehydrogenase (LDH)	<10%- very low risk of mortality >30%- high risk of mortality	van Dam 0.77 (0.73, 0.81) van Dam 0.83 (0.79, 0.88)	P(30-day mortality)=1/(1+exp (-(−2.083+0.795 * (0.050*Age +1.115*≥2 Abnormal Vital Signs (yes=1, no=0)–0.112*Albumin (in g/L) +0.284* (BUN (in mmol/L)/5) +0.120* (LDH (in U/L)/100)+0.875* Bilirubin>20 µmol/L (yes=1, no=0))))
Quick Sepsis-related Organ Failure Assessment (qSOFA) Artero [17] (Spain) Bradley [21] (UK) Gupta [27] (UK) Liu FY [30] (China) **Neto (Spain, Brazil)**	Inpatients	Mortality (in-hospital)	Mental status (GCS) RR Systolic blood pressure (SBP)		Artero 0.73 (0.71, 0.74) Bradley 0.62 Gupta 0.6 (0.54, 0.65) Liu FY 0.69 (0.64, 0.75) **Neto 0.63 (0.6,0.66)**	https://www.mdcalc.com › qsofa-quick-sofa-score-sepsis
National Early Warning Score 2 (NEWS2) Baker [18] (UK)	Inpatients on admission	Risk of clinical deterioration (CD)	RR PR Hypercapneic respiratory failure		Baker 0.7 (0.65, 0.77) Gupta 0.69 (0.68, 0.70) Carr • CD in 3 days 0.72,0.77	https://www.mdcalc.com/national-early-warning-score-news-2

Bradley [21] (UK) Carr [22] (UK) Gupta [27] (UK) Gupta [14] (UK)			Room air or with supplemental O2 Temp SBP Consciousness		• CD in 14 days 0.70, 0.74 Gupta • CD in 1-day 0.78 (0.73, 0.83)	
Modified Early Warning Score (MEWS) Gupta [27] (UK) Gupta [14] (UK)	Inpatients	Risk of clinical deterioration	SBP Heart rate (HR) RR Temperature Alert Voice Response Pain Response Unresponsive (AVPU) score		Gupta 0.6 (0.56, 0.65) Gupta 0.63 (0.62, 0.64)	https://www.mdcalc.com/modified-early-warning-score-mews-clinical-deterioration
COVID-GRAM **Armiñanzas [51] (Spain)** **Liang [61] (China)** **Doganay [55] (Turkey)** **Neto [61] (Brazil)**	Inpatients	Critical illness 30-day mortality ICU requirement	X-ray abnormality Age Hemoptysis Dyspnea Unconsciousness Number of comorbidities Cancer history Neutrophil/Lymphocytes (NLR) Lactate Dehydrogenase (LDH) Direct Bilirubin	<1.7% - Low 1.7% to <40.4% - Medium >/= 40.4% - High	**Armiñanzas** • **critical illness 0.779** • **30-day mortality 0.88** **Liang** • **DC 0.88 (0.85-0.91)** **Liang** • **VC 0.88 (0.84-0.93)** **Doganay** • **mortality, 0.701 (0.658, 0.742)** • **ICU requirement 0.684 (0.640-0.725)** **Neto** • **0.77 (0.75-0.8)**	https://www.mdcalc.com/covid-gram-critical-illness-risk-score
Clinical Frailty Scale **Apea [49] (UK)** **Cobos-Siles [53] (Spain)** **Dres [55] (France)** **Miles [62] (UK)** **Aw [51] (UK)** **Jung [46] (Germany)** **Aliberti [48] (Brazil)** **Hewitt [58] (UK) (Italy)** **Thompson [63] (UK)**	Inpatients	30-day mortality Day 90 mortality Survival at 30 days Death within 30 days and 6 months of hospital admission	Clinical Frailty Scale		**Apea** • **RCFS Asian 1.98 (1.37, 2.86)** **Black** • **1.67 (1.14, 2.45)** **Cobos-Siles** • **8.73 (1.37-55.46)** **Dres** • **CFS 4 Univariate HR 2.14 (1.71, 2.68) Multivariate HR 2.24 (1.63, 3.09)** • **CFS 5 Univariate 2.81 (2.17, 3.64) Multivariate 2.83 (1.96, 4.08)** **Miles** • **CFS Univariate HR 1.12 (1.02, 1.23) Multivariate HR 1.88 (1.37, 2.59)** • **CFS x COVID-19 Multivariate HR 0.51 (0.27, 0.71)** **Aw** • **CFS 4 HR 1.23 (0.73, 2.07)**	https://www.mdcalc.com/csha-clinical-frailty-scale-cfs

					• **CFS 5 HR 1.18 (0.70, 1.99)** • **CFS 6 2.20 (1.41, 3.43) CFS 7-9 2.20 (1.41, 3.43)** **Jung** • **3.20 (2.56, 4.13)** • **2.41 (1.77, 3.27)** • **1.86 (1.36, 2.52)** **Aliberti** **30-day mortality** • **CFS 4 1.4 (1.1, 1.7)** • **CFS 5 1.5 (1.1, 1.9)** • **CFS 6 1.8 (1.4, 2.3)** • **CFS 7-9 2.1 (1.6, 2.7)** **6-month mortality** • **CFS 4 1.4 (1.1, 1.7)** • **CFS 5 1.5 (1.1, 1.8)** • **CFS 6 1.9 (1.5, 2.4)** • **CFS 7-9 2.3 (1.8, 2.9)** **Hewitt** • **CFS 3-4 1.55 (1.00, 2.41)** • **CFS 5-6 (1.83 (1.15, 2.91)** • **CFS 7-9 2.39 (1.5, 3.81)** **Thompson** • **Median CFS OR 1.72 (1.52, 1.94)**	

**Discrimination performance: ability of the model to discriminate between those who will and will not develop the outcome of interest. An area under the curve (AUC) of 0.90-1.0 indicates excellent discriminatory capacity of the model; 0.80-0.90 good; 0.70-0.80 fair; 0.60-0.70 poor; <0.60 failure to discriminate.*
**Hazard ratio: a hazard ratio greater than 1 suggests an increased risk, below 1 suggests a smaller risk*

References

[1] Jin Y, Yang H, Ji Wangquan, Wu Weidong, Chen S, Zhang W, Guangcai D. Virology, Epidemiology, Pathogenesis, and Control of COVID-19. Viruses. 2020;12(372):1–17.

[2] DOH COVID-19 Bulletin #374. https://doh.gov.ph/covid19casebulletin374. Accessed on March 23, 2021.

[3] Miller J, Tada M, Goto M, Mohr N, Lee S. Prediction Models for Severe Manifestations and Mortality due to COVID-19: a Rapid Systematic Review. medRxiv preprint doi: https://doi.org/10.1101/2021.01.28.21250718; this version posted February 1, 2021.

[4] Wynants L, Van Calster B, Collins G, Riley R, Heinze G, Schuit E et al. Prediction models for diagnosis and prognosis of covid-19: systematic review and critical appraisal. BMJ 2020;369:m1328 http://dx.doi.org/10.1136/bmj.m1328

[5] Moons KGM, de Groot JAH, Bouwmeester W, Vergouwe Y, Mallett S, Altman DG, et al. (2014) Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies: The CHARMS Checklist. PLoS Med 11(10): e1001744. https://doi.org/10.1371/journal.pmed.1001744

[6] Moons KGM, Wolff RF, Riley RD, Whiting PF, Westwood M, Collins GS, Reitsma JB, Kleijnen J, Mallett S. PROBAST: A Tool to Assess Risk of Bias and Applicability of Prediction Model Studies: Explanation and Elaboration. Ann Intern Med. 2019 Jan 1;170(1):W1-W33. doi: 10.7326/M18-1377. PMID: 30596876.

[7] Williamson 2021. Williamson E, Tazare J, Bhaskaran K, H McDonald, Walker A, Tomlinson L, OpenSAFELY Collaborative. Predicting COVID-19 related death using the OpenSAFELY platform. medRxiv preprint doi: https://doi.org/10.1101/2021.02.25.21252433; this version posted March 1, 2021.

[8] WHO weekly epidemiological update- 29 December 2020. https://www.who.int/publications/m/item/weekly-epidemiological-update---29-december-2020. Accessed on March 31, 2021.

[9] Clift AK, Coupland CAC, Keogh RH, Diaz-Ordaz K, Williamson E, Harrison EM et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 2020;371:m3731 http://dx.doi.org/10.1136/bmj.m3731

[10] Nafilyan V, Humberstone B, Mehta N, Diamond I, Coupland C, Lorenzi L et al. An external validation of the QCovid risk prediction algorithm for risk of mortality from COVID-19 in adults: national validation cohort study in England. medRxiv preprint https://doi.org/10.1101/2021.01.22.21249968 this version posted January 25, 2021

[11] Jimenez-Solem E et al. Developing And Validating Covid-19 Adverse Outcome Risk Prediction Models From A Bi-National European Cohort Of 5594 Patients. doi: https://doi.org/10.1101/2020.10.06.20207209

[12] Knight SR, Ho A, Pius R, Buchan I, Carson G, Drake TM, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ. 2020;370:m3339.

[13] Marcolino M, Pires M, Ramos L, Silva R, Oliveira L, Carvalho R, et al. ABC2-SPH risk score for in-hospital mortality in COVID-19 patients: development, external validation and comparison with other available scores. medRxiv preprint doi: https://doi.org/10.1101/2021.02.01.21250306; this version posted February 3, 2021

[14] Gupta R, Harrison E, Ho A, Docherty A, Knight S, Smeden M et al. Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study. Lancet Respir Med 2021.https://doi.org/10.1016/S2213-2600(20)30559-2

[15] Adderley N, Taverner T, Price M, Sainsbury C, Greenwood D, Chandan J et al. Development and external validation of prognostic models for COVID-19 to support risk stratification in secondary care.

medRxiv preprint doi: https://doi.org/10.1101/2021.01.25.21249942; this version posted January 30, 2021.

[16] Ageno W, Cogliati C, Perego M, Girelli D, Crisaffuli E, Pizzolo F et al. Clinical risk scores for the early prediction of severe outcomes in patients hospitalized for COVID-19. Internal and Emergency Medicine 2020. https://doi.org/10.1007/s11739-020-02617-4

[17] Artero A, Madrazo M, Fernandez-Garces M, Miguez A, Garcia A, Vieitez ASeverity Scores in COVID-19 Pneumonia: a Multicenter, Retrospective, Cohort Study. J Gen Intern Med DOI: 10.1007/s11606-021-06626-7.

[18] Baker KF, Hanrath A, van der Loeff I, Kay L, Back J, Duncan C. National Early Warning Score 2 (NEWS2) to identify inpatient COVID-19 deterioration: a retrospective analysis. Clinical Medicine 2021, Vol 21 No 2 March 2021.

[19] Bartoletti M, Giannella M, Scudeller L, Tedeschi S, Rinaldi M, Bussini L et al. Development and validation of a prediction model for severe respiratory failure in hospitalized patients with SARS-CoV-2 infection: a multicentre cohort study (PREDI-CO study). Clinical Microbiology and Infection. 2020 https://doi.org/10.1016/j.cmi.2020.08.003.

[20] Berenguer J, Borobia A, Ryan P, Rodriguez-Bano J, Bellon J, Harrin I et al. Development and validation of a prediction model for 30-day mortality in hospitalised patients with COVID-19: the COVID-19 SEIMC score. Thorax 2020. http://dx.doi.org/10.1136/ thoraxjnl-2020-216001).

[21] Bradley P, Frost F,Tharmaratnam K, et al. Utility of established prognostic scores in COVID-19 hospital admissions: multicenter prospective evaluation of CURB-65, NEWS2 and qSOFA. BMJ Open Resp Res 2020;7:e000729. doi:10.1136. bmjresp-2020-000729.

[22] Carr E, Bendayan R, Bean D, Stammers M. Wang W, Zhang H, Searle T et al. Evaluation and improvement of the NEWS2 for COVID-19: a multi-hospital study. BMC Medicine 19:23. https://doi.org/10.1186/s12916-020-01893-3.

[23] Castro V, McCoy T, Perlis R. Consistency of performance of adverse outcome prediction models for hospitalized COVID-19 patients. medRxiv preprint doi: https://doi.org/10.1101/2021.02.25.21252410; this version posted March 1, 2021.

[24] Chua F, Vancheeswaran R, Draper A*, Vaghela T, Knight M, Mogal R et al.* Early prognostication of COVID-19 to guide hospitalisation versus outpatient monitoring using a point-of-test risk prediction score*Thorax* Published Online First: 10 March 2021. doi: 10.1136/thoraxjnl-2020-216425

[25] Codon J, Lip G, Rey H, Iniesta A, Rosillo S, Castrejon S et al. Prediction of thromboembolic events and mortality by the $CHADS_2$ and the CHA_2DS_2-VASc in COVID-19. Europace (2021) 00, 1–11 doi:10.1093/europace/euab015.

[26] El-Solh AA, Lawson Y, Carter M, El-Solh DA, Mergenhagen KA (2020) Comparison of in-hospital mortality risk prediction models from COVID-19. PLoS ONE 15(12): e0244629. https://doi.org/10.1371/journal.pone.0244629

[27] Gupta RK, Marks M, Samuels THA, et al. Systematic evaluation and external validation of 22 prognostic models among hospitalised adults with COVID-19: An observational cohort study. Eur Respir J 2020; in press (https://doi.org/10.1183/13993003.03498-2020).

[28] King JT, Jr., Yoon JS, Rentsch CT, Tate JP, Park LS, Kidwai-Khan F, et al. (2020) Development and validation of a 30-day mortality index based on pre-existing medical administrative data from 13,323 COVID-19 patients: The Veterans Health Administration COVID-19 (VACO) Index.PLoS ONE 15(11): e0241825. https://doi.org/10.1371/journal.pone.0241825

[29] Li, J., Chen, Y., Chen, S. *et al.* Derivation and validation of a prognostic model for predicting in-hospital mortality in patients admitted with COVID-19 in Wuhan, China: the PLANS (platelet lymphocyte age neutrophil sex) model. *BMC Infect Dis* 20, 959 (2020). https://doi.org/10.1186/s12879-020-05688-y

[30] Fang-Yan Liu, Xue-Lian Sun, Yong Zhang, Lin Ge, Jing Wang, Xiao Liang, Jun-Fen Li, Chang-Liang Wang, Zheng-Tao Xing, Jagadish K. Chhetri, Peng Sun, Piu Chan. Evaluation of the Risk Prediction

Tools for Patients With Coronavirus Disease 2019 in Wuhan, China: A Single-Centered, Retrospective, Observational Study. Critical Care Medicine DOI: 10.1097/CCM.0000000000004549

[31] Liu H, Chen J, Yang Q, Wang Y, Cai J, Li H. Development and validation of a risk score using complete blood count to predict in-hospital mortality in COVID-19 patients, Med (2020), https://doi.org/10.1016/j.medj.2020.12.013

[32] Mancilla-Galindo J, Vera- Zertuche JM, Navarro-Cruz AR, Segura-Badilla O, Reyes-Velázquez G, Tepepa-López FJ, Aguilar-Alonso P, Vidal-Mayo JdeJ, Kammar- García A (2020). Development and validation of the patient history COVID-19 (PH-Covid19) scoring system: a multivariable prediction model of death in Mexican patients with COVID-19. Epidemiology and Infection 148, e286, 1–8. https://doi.org/10.1017/ S095026882000290

[33] Guillermo Rodriguez-Nava, Maria Adriana Yanez-Belloa, Daniela Patricia Trelles-Garciaa, Chul Won Chunga, Harvey J. Friedmanb,c, David W. Hinesd. Performance of the quick COVID-19 severity index and the Brescia-COVID respiratory severity scale in hospitalized patients with COVID-19 in a community hospital setting. International Journal of Infectious Diseases 102 (2021) 571–576

[34] Nicholson C, Wooster L, Sigurslide H, Li R, Jiang W, Tian W, Cardenas C, Malhotra R. Estimating risk of mechanical ventilation and in-hospital mortality among adult COVID-19 patients admitted to Mass General Brigham: The VICE and DICE scores. EClinicalMedicine 33 (2021) 100765

[35] Paranjape N, Staples L, Stradwick C, Ray H, Saldanha I. Development and validation of a predictive model for critical illness in adult patients requiring hospitalization for COVID-19 medRxiv preprint doi: https://doi.org/10.1101/2021.01.22.21250289; this version posted January 22, 2021.

[36] Richardson D, Faisal M, Fiori M, *et al*. Use of the first National Early Warning Score recorded within 24 hours of admission to estimate the risk of in-hospital mortality in unplanned COVID-19 patients: a retrospective cohort study. *BMJ Open* 2021;11:e043721. doi:10.1136/bmjopen-2020-043721

[37] Schöning V, Liakoni E, Baumgartner C, Exadaktylos A, Hautz W, Atkinson A, Hammann F Development and validation of a prognostic COVID-19 severity assessment (COSA) score and machine learning models for patient triage at a tertiary hospital*. J Transl Med (2021) 19:56* https://doi.org/10.1186/s12967-021-02720-w

[38] Tanboga IH, Canpolat U, Çetin E, Kundi H, Çelik O, Çağlayan M, Ata N, Özeke O, Çay S, Kaymaz C, Topaloğlu S. Development and validation of clinical prediction model to estimate the probability of death in hospitalized patients with COVID-19: Insights from a nationwide database. J Medical Virology 2021;1–8 DOI: 10.1002/jmv.26844

[39] van Dam P, Zelis N, van Kuijk S, Linkens A, Bruggemann R, Spaetgens B et al. Performance of prediction models for short term outcome in COVID-19 patients in the emergency department: a retrospective study. Ann Med 2021 Dec;53(1):402-409. doi: 10.1080/07853890.2021.1891453

[40] van Dam PMEL, Zelis N, Stassen P, *et al*. Validating the RISE UP score for predicting prognosis in patients with COVID-19 in the emergency department: a retrospective study. *BMJ Open* 2021;11:e045141. doi:10.1136/bmjopen-2020-045141

[41] van Klaveren D, Rekkas A, Alsma J, Verdonschot R, Koning D, Kamps M et al. COVID Outcome Prediction in the Emergency Department (COPE): Development and validation of a model for predicting death and need for intensive care in COVID-19 patients. medRxiv preprint doi: https://doi.org/10.1101/2020.12.30.20249023; this version posted February 8, 2021

[42] National COVID-19 Clinical Evidence Task Force. Living Guidelines. https://covid19evidence.net.au/

[43] World Health Organization. (2021, December 7). *Therapeutics and covid-19: Living guideline*. World Health Organization. Retrieved December 7, 2021, from https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.3.

[44] Sun JG. A Novel Nomogram to Predict Severity of COVID-19. 2020 Apr 28 [last updated 2020 Jul 14; cited 2021 Apr 8]. In: [Internet]. Bethesda (MD): U.S. National Library of Medicine. 2020 - Available from: https://clinicaltrials.gov/ct2/show/NCT04366024?term=prediction+model&cond=Covid19&draw=3&rank=15

[45] Twerenbold R, Pfister GK, et al. COVID-19 Survival - The COVIVA Study (COVIVA). 2020 Apr 29 [last updated 2020 May 4; cited 2021 Apr 8]. In: [Internet]. Bethesda (MD): U.S. National Library of Medicine. 2020 - Available from: https://clinicaltrials.gov/ct2/show/NCT04366765

[46] Jung C. Outcomes and Prognostic Factors in COVID-19 (COVIP). 2020 Mar 25 [last updated 2020 Dec 19; cited 2021 Apr 8]. In: [Internet]. Bethesda (MD): U.S. National Library of Medicine. 2020 - Available from: https://clinicaltrials.gov/ct2/show/NCT04321265

[47] Morello F. Risk Stratification of COVID-19 Patients Discharged From the Emergency Department (CODED). 2020 Nov 16 [last updated 2021 Feb 9; cited 2021 Apr 8]. In: [Internet]. Bethesda (MD): U.S. National Library of Medicine. 2020 - Available from: https://clinicaltrials.gov/ct2/show/NCT04629183?term=CODED&cond=Covid19&draw=2&rank=1

[48] Morello F. Risk Stratification of COVID-19 Patients Discharged From the Emergency Department (CODED). 2020 Nov 16 [last updated 2021 Feb 9; cited 2021 Apr 8]. In: [Internet]. Bethesda (MD): U.S. National Library of Medicine. 2020 - Available from: https://clinicaltrials.gov/ct2/show/NCT04629183?term=CODED&cond=Covid19&draw=2&rank=1

[49] Aliberti, M. J., Szlejf, C., Avelino-Silva, V. I., Suemoto, C. K., Apolinario, D., Dias, M. B., Garcez, F. B., Trindade, C. B., Amaral, J. R., Melo, L. R., Aguiar, R. C., Coelho, P. H., Hojaij, N. H., Saraiva, M. D., Silva, N. O., Jacob-Filho, W., & Avelino-Silva, T. J. (2021). Covid -19 is not over and age is not enough: Using frailty for prognostication in hospitalized patients. *Journal of the American Geriatrics Society*, *69*(5), 1116–1127. https://doi.org/10.1111/jgs.17146

[50] Apea, V. J., Wan, Y. I., Dhairyawan, R., Puthucheary, Z. A., Pearse, R. M., Orkin, C. M., & Prowle, J. R. (2020). Ethnicity and outcomes in patients hospitalised with COVID-19 infection in East London: An observational cohort study. *Medrxiv*. https://doi.org/10.1101/2020.06.10.20127621

[51] Armiñanzas, C., Arnaiz de las Revillas, F., Gutiérrez Cuadra, M., Arnaiz, A., Fernández Sampedro, M., González-Rico, C., Ferrer, D., Mora, V., Suberviola, B., Latorre, M., Calvo, J., Olmos, J. M., Cifrián, J. M., & Fariñas, M. C. (2021). Usefulness of the covid-gram and curb-65 scores for predicting severity in patients with covid-19. *International Journal of Infectious Diseases*, *108*, 282–288. https://doi.org/10.1016/j.ijid.2021.05.048

[52] Aw, D., Woodrow, L., Ogliari, G., & Harwood, R. (2020). Association of frailty with mortality in older inpatients with COVID-19: A cohort study. *Age and Ageing*, *49*(6), 915–922. https://doi.org/10.1093/ageing/afaa184

[53] Cobos-Siles, M., Cubero-Morais, P., Arroyo-Jiménez, I., Rey-Hernández, M., Hernández-Gómez, L.Vargas-Parra, D. J., González-Fernández, M., Cazorla-González, M., Gabella-Martín, M., Ruíz-Albi, T., Berezo-García, J. A., García-Cruces-Méndez, J. F., Miramontes-González, J. P., & Corral-Gudino, L. (2020). Cause-specific death in hospitalized individuals infected with SARS-COV-2: More than just acute respiratory failure or thromboembolic events. *Internal and Emergency Medicine*, *15*(8), 1533–1544. https://doi.org/10.1007/s11739-020-02485-y

[54] Diebold, M., Zimmermann, T., Dickenmann, M., Schaub, S., Bassetti, S., Tschudin-Sutter, S., Bingisser, R., Heim, C., Siegemund, M., Osswald, S., Kuster, G. M., Rentsch, K. M., Breidthardt, T., & Twerenbold, R. (2021). Comparison of acute kidney injury in patients with covid-19 and other respiratory infections: A prospective cohort study. *Journal of Clinical Medicine*, *10*(11), 2288. https://doi.org/10.3390/jcm10112288

[55] Doğanay, F., & Ak, R. (2021). Performance of the curb-65, Isaric-4C and covid-gram scores in terms of severity for Covid-19 patients. *International Journal of Clinical Practice*, *75*(10). https://doi.org/10.1111/ijcp.14759

[56] Dres, M., Hajage, D., Lebbah, S., Kimmoun, A., Pham, T., Béduneau, G., Combes, A., Mercat, A., Guidet, B., Demoule, A., & Schmidt, M. (2021). Characteristics, management, and prognosis of elderly patients with covid-19 admitted in the ICU during the first wave: Insights from the Covid-ICU Study. *Annals of Intensive Care*, *11*(1). https://doi.org/10.1186/s13613-021-00861-1

[57] Dumitrascu, F., Branje, K. E., Hladkowicz, E. S., Lalu, M., & McIsaac, D. I. (2021). Association of frailty with outcomes in individuals with covid -19: A living review and meta-analysis. *Journal of the American Geriatrics Society*, *69*(9), 2419–2429. https://doi.org/10.1111/jgs.17299

[58] Goodacre, S., Thomas, B., Sutton, L., Burnsall, M., Lee, E., Bradburn, M., Loban, A., Waterhouse, S., Simmonds, R., Biggs, K., Marincowitz, C., Schutter, J., Connelly, S., Sheldon, E., Hall, J., Young, E., Bentley, A., Challen, K., Fitzsimmons, C., … Walter, D. (2021). Derivation and validation of a clinical severity score for acutely ill adults with suspected covid-19: The Priest Observational Cohort Study. *PLOS ONE*, *16*(1). https://doi.org/10.1371/journal.pone.0245840

[59] Hewitt, J., Carter, B., Vilches-Moraga, A., Quinn, T. J., Braude, P., Verduri, A., Pearce, L., Stechman, M., Short, R., Price, A., Collins, J. T., Bruce, E., Einarsson, A., Rickard, F., Mitchell, E., Holloway, M., Hesford, J., Barlow-Pay, F., Clini, E., … Guaraldi, G. (2020). The effect of frailty on survival in patients with covid-19 (COPE): A multicentre, European, observational cohort study. *The Lancet Public Health*, *5*(8). https://doi.org/10.1016/s2468-2667(20)30146-8

[60] Jung, C., Flaatten, H., Fjølner, J., Bruno, R. R., Wernly, B., Artigas, A., Bollen Pinto, B., Schefold, J. C., Wolff, G., Kelm, M., Beil, M., Sviri, S., van Heerden, P. V., Szczeklik, W., Czuczwar, M., Elhadi, M., Joannidis, M., Oeyen, S., Zafeiridis, T., … Zegers, M. (2021). The impact of frailty on survival in elderly intensive care patients with covid-19: The COVIP study. *Critical Care*, *25*(1). https://doi.org/10.1186/s13054-021-03551-3

[61] Lazar Neto, F., Marino, L. O., Torres, A., Cilloniz, C., Meirelles Marchini, J. F., Garcia de Alencar, J. C., Palomeque, A., Albacar, N., Brandão Neto, R. A., Souza, H. P., Ranzani, O. T., Bortolotto, A. L., Müller Veiga, A. D., Bellintani, A. P., Fantinatti, B. L., Nicolao, B. R., Caldeira, B. T., Umehara Juck, C. E., Bueno, C. G., … Gomez Gomez, L. M. (2021). Community-acquired pneumonia severity assessment tools in patients hospitalized with COVID-19: A validation and clinical applicability study. *Clinical Microbiology and Infection*, *27*(7). https://doi.org/10.1016/j.cmi.2021.03.002

[62] Liang, W., Liang, H., Ou, L., Chen, B., Chen, A., Li, C., Li, Y., Guan, W., Sang, L., Lu, J., Xu, Y., Chen, G., Guo, H., Guo, J., Chen, Z., Zhao, Y., Li, S., Zhang, N., Zhong, N., & He, J. (2020). Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with covid-19. *JAMA Internal Medicine*, *180*(8), 1081. https://doi.org/10.1001/jamainternmed.2020.2033

[63] Miles, A., Webb, T. E., Mcloughlin, B. C., Mannan, I., Rather, A., Knopp, P., & Davis, D. (2020). Outcomes from covid-19 across the range of frailty: Excess mortality in fitter older people. *European Geriatric Medicine*, *11*(5), 851–855. https://doi.org/10.1007/s41999-020-00354-7

[64] Thompson, J. V., Meghani, N. J., Powell, B. M., Newell, I., Craven, R., Skilton, G., Bagg, L. J., Yaqoob, I., Dixon, M. J., Evans, E. J., Kambele, B., Rehman, A., & Ng Man Kwong, G. (2020). Patient characteristics and predictors of mortality in 470 adults admitted to a District General Hospital in England with covid-19. *Epidemiology and Infection*, *148*. https://doi.org/10.1017/s0950268820002873

Appendix 1. Evidence to Decision

Table 1. Summary of initial judgements prior to the panel discussion (N = 4)

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Problem	No (1)	Yes (3)					In order to reduce the risk of severe disease and mortality, numerous studies have assessed the usefulness of prognostic models that aim to identify patients at high risk of adverse outcomes from COVID-19.
Certainty of Evidence	High	Moderate	Low (2)	Very low (2)			Thirty-three (36) cohort studies on prognostic models for clinical deterioration and mortality of individuals with COVID-19 were found. Most of the studies (n = 31) were assessed to have high risk of bias due to issues in participant selection and analysis. For predicting mortality, the following models demonstrated fair-to-good predictive ability: 4C mortality score, ABC2-SPH, CURB-65, REMS, RISE UP and COVID-GRAM models. Poor to fair prediction was noted for the qSOFA model. Only one model, the QCOVID model for mortality validated for the UK setting, demonstrated high predictive ability but this model has been validated in the UK setting. For predicting clinical deterioration, available prognostic models showed varied performance. The 4C deterioration which has been investigated in only one study with low risk of bias, showed fair predictive ability. The MEWS model has poor prediction of clinical deterioration while NEWS2 has inconsistent prediction (poor to good). The Clinical Frailty Scale (CFS), increases the risk of mortality among elderly COVID-19 patients.
Accuracy	Very Accurate	Accurate	Inaccurate (4)	Very Inaccurate	Uncertain		

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Values	Important uncertainty or variability	Possibly important uncertainty or variability (1)	Possibly NO important uncertainty or variability (3)	No important uncertainty or variability			No research evidence found.
Resources Required	Uncertain (2)	Large cost (1)	Moderate Cost	Negligible cost or savings (1)	Moderate savings	Large savings	
Certainty of evidence of required resources	No included studies (2)	Very low (1)	Low (1)	Moderate	High		
Cost effectiveness	No included studies (3)	Favors using comparator	Does not favor either using prognostic models or the comparator (1)	Favors the prognostic models			
Equity	Uncertain (2)	Reduced	Probably no impact (1)	Increased (1)			
Acceptability	Uncertain (2)	No	Yes (2)				
Feasibility	Uncertain (2)	No	Yes (2)				

Appendix 2. Characteristics of Included Studies

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
Adderley 2021 [15]	Retrospective cohort UK Jan 1-Sep 12, 2020 Last admission on Aug 16, 2020	28-day outcomes Mortality Training cohort (TC) n=288 (7.48%) Validation cohort (VC) n=1668 (27.35%) Admission to intensive care unit (ICU) TC, n= 183 (4.75%) VC, n= 722 (12.66%)	Admission or up to 72h from admission	TC Inpatients RT-PCR positive (RT-PCR+) n = 3849 VC RT-PCR+ or antibody test-positive n=6099	Demographic features Clinical features Laboratory features Imaging Frailty score Glasgow Coma Score (GCS) Comorbidity 63 candidate predictors for model development 27 candidate predictors in external validation population	Literature review Discussion with experts Available collected variables Time series analysis	Mortality model: Age, breathlessness, sputum, systolic blood pressure (SBP),Temperature (temp), Respiratory rate (RR), Oxygen saturation (O2sat) , FiO2, alkaline phosphatase (ALP), C-reactive protein (CRP), Calcium, Eosinophils, Glucose, pH, Urea, WBC count, platelets, and frailty score ICU admission model: age, gender, fever, new onset diarrhoea or vomiting, heart rate (HR),RR, FiO2, temp Albumin, CRP, eGFR, pH, monocytes, WBC, frailty score, and GCS Reduced model: Age, SBP, temp, RR, O2 sat, FiO2,	TC Mortality 0.778 (0.741, 0.815) ICU admission 0.892 (0.865, 0.920) Reduced model Mortality TC 0.791 (0.761, 0.822); VC 0.767 (0.754, 0.780) ICU admission TC 0.906 (0.883, 0.929) VC 0.811 (0.795, 0.828)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
							frailty score, pH,urea, CRP	
Ageno 2020 [16] Italy	Retrospective cohort Five centers Feb 17 - May 8, 2020	Severe outcome defined as non-invasive ventilation (NIV), intubation , or death n= 275 (45.08%)	Admission	Inpatients RT-PCR+ n = 610	Demographic features Comorbidity Laboratory tests	No explanation for selection Multivariate logistic regression with backward selection, LASSO, Random Forest	Age Coronary heart disease PCR, AST, D-dimer, NLR 6 variables 13 points	0.80 Cut-off 7 points in VCt Sensitivity0.93 Specificity 0.34 PPV 0.59 NPV 0.82.
Aliberti 2021 CFS Brazil	Retrospective cohort Hospital das Clinicas, Brazil March 30 to July 7, 2020	Time to death within 30 days and 6 months of hospital admission	Admission	Inpatients age 50 or more, RT PCR+ and serologic N = 1830	n/a	n/a	CFS	30-day mortality CFS 1-3 reference 4 crude HR 1.5 (1.2-1.9) adjusted HR 1.4 (1.1-1.7) 5 crude HR 1.9 (1.5-2.4) adjusted HR 1.5 (1.1-1.9) 6 crude HR 2.3 (1.8-2.9) adjusted HR 1.8 (1.4-2.3) 7-9 crude HR 2.6 (2.1-3.4) adjusted HR 2.1 (1.6-2.7) 6-month mortality CFS 1-3 reference 4 crude HR 1.5 (1.2-1.8) adjusted HR 1.4 (1.1-1.7)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
								5 crude HR 1.9 (1.6-2.4) adjusted HR 1.5 (1.1-1.8) 6 crude HR 2.3 (1.8-2.9) adjusted HR 1.9 (1.5-2.4) 7-9 crude HR 2.6 (2.1-3.4) adjusted HR 2.1 (1.8-2.9)
Apea et al. 2020 CFS UK	Prospective 5 acute hospitals May 20 2020	30-day mortality	Admission	Inpatients RT PCR + n = 1996	n/a	n/a	CFS	RCFS Asian 1.98 (1.37-2.86) Black 1.67 (1.14-2.45)
Armiñanzas 2021 COVID GRAM CURB-65 Spain	Retrospective Hospital Universitario Marques de Valdecilla February to May 2020	Critical illness as a composite endpoint of ICU admission and 30-day mortality N=110 (21.0%)	Admission	Adult inpatients RT PCR+ N=523	n/a	n/a	COVID-GRAM CURB-65	CURB-65 0.727 COVID-GRAM 0.88
Artero et al., 2020 [17] Spain	Retrospective cohort Multi-center March- May 2020	Mortality, all-cause n= 2135 (20.9%) ICU/mechanical ventilation n=907 (8.9%)	Admission	Inpatients RT-PCR+/ antibody+ n =10,238	N/A	N/A	Pneumonia Severity Index CURB-65 qSOFA (altered mental status, RR, SBP) MuLBSTA: Age, smoking, bacteria infection, HPN Lymphocytes	*Mortality* PSI 0.835 (0.826, 0.845) CURB-65 0.825 (0.815, 0.835) MuLBSTA 0.715 (0.703, 0.727) qSOFA: 0.728 (0.715, 0.741) *ICU admission* PSI 0.539 (0.521, 0.557) CURB-65 0.562 (0.544, 0.580)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
							Imaging-multilobar infiltrates	MuLBSTA 0.658 (0.640, 0.677) qSOFA 0.616 (0.598, 0.635) *Mechanical ventilation* PSI 0.560 (0.540, 0.579) CURB-65 0.572 (0.553, 0.592) MuLBSTA 0.678 (0.657, 0.698) qSOFA 0.624 (0.603, 0.644)
Aw et al. 2020 CFS UK	Retrospective March 1 2020 to April 30 2020	all-cause mortality	Admission	Inpatients diagnosed with COVID-19 n=677	n/a	n/a	CFS	Aw CFS 4 HR 1.23 (0.73-2.07) CFS 5 HR 1.18 (0.70-1.99) CFS 6 2.20 (1.41-3.43) CFS 7-9 2.20 (1.41-3.43)
Baker 2021 [18] UK	Retrospective cohort Single-center Jan- Apr, 2020	Clinical deterioration defined as initiation of NIV or mechanical ventilation (MV), ICU admission, end of care, or in-hospital death *Data censored at 28 days for patients still admitted n= 133 (44.9%)	Admission	Inpatients RT-PCR+ n = 296 131 with severe covid on admission	N/A	N/A	NEWS2:HR, BP, temp, RR, O2 sat, level of consciousness	0.70 (0.65–0.77)
Bartoletti 2020 [19] Italy	Retrospective cohort study Multi- centre	Severe respiratory failure- SpO2 <93% with 100%	Admission	Inpatients RT-PCR+ n = 1113	Demographic,Comorbidities Symptoms on	No explanation	PREDI-CO score: Age Obesity, RR Fever at	0.85 (0.81-0.88)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
	Feb- April, 2020	FiO2, RR>30/ min or respiratory distress n=367 (32.97%)			admission Laboratory tests		hospitalization Lymphocytes Creatinine, CRP, LDH	
Berenguer 2021 [20] Spain	Retrospective cohort Feb- April, 2020	30-day mortality n= 341 (5.5%)	Admission	Inpatients RT-PCR+ n = 6161	Demographic ComorbiditiesSigns and symptoms Laboratory tests	17 baseline variables found to be independently associated with death in the COVID-19 Spain cohort	COVID-19 SEIMC score Age, sex Dyspnea, age-adjusted SaO2 NLR, eGFR by CKD-EPI	0.831 (0.806–0.856)
Bradley 2020 [21] UK	Prospective Seven respiratory hospitals in NW England April 1-14, 2020	30-day mortality n=300 (36.14%) ICU admission n=142 (17.10%)	Admission	Consecutive adults admitted meeting the Public Health England inpatient case definition for COVID-19 and PCR+ n=800			CURB-65 NEWS2 qSOFA	30-day mortality CURB-65- 0.75 NEWS2- 0.67 qSOFA- 0.62 72-h mortality CURB-65- 0.76 NEWS2- 0.78 qSOFA 0.65 ICU admission CURB-65 0.63 NEWS2 0.65 qSOFA 0.55
Carr 2021 [22] UK	Retrospective cohort study Multi- center Feb-Aug, 2020	Severe covid-19 outcomes (transfer to ICU or death at 3 and 14 days from admission or symptom onset for nosocomial COVID TC 3-day n = 389 (30.48%) 14-day n= 163 VC 3-day n= 27-289 14-day n=39-391	Admission (up to 48h after admission)	Inpatients RT-PCR+ n = 7513 TC, n = 1276 (1 hospital of NHS Hospitals Trust) C,n = 6237 (5 centers of NHS Hospitals Trust, 1 hospital in Norway, 2 hospitals in Wuhan, China)	Age, sex, ethnicity, select comorbidity, physiologic measures (NEWS2), biomarkers (alb, CRP, GFR, lymphocyte ct, neutrophil ct, platelet ct, NLR, lym-CRP ratio, urea)	routinely obtained parameters available in a wide range of settings Regularised logistic regression with least absolute shrinkage & selection operator (LASSO) estimator	Model 1: NEWS2 only Model 2: NEWS2 + age Model 3: Supplemented NEWS2 score Age Supplemental O2 flow rate, O2 sat, eGFR Urea, CRP, Neutrophil count NLR	NEWS2 3-day: 0.717-0.772 14-day: 0.697-0.743 NEWS+age 3-day: 0.717-0.772 14-day severe outcome: 0.686-0.815 All features 3-day: 0.716-0.831 14-day: 0.762-0.864 *All models showed evidence of increasing

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
								miscalibration as new predictors are added to the model
Castro 2021 [23] USA	Retrospective cohort study Multi- center- 2 academic centers and 4 commu-nity hospitals June 7, 2020-Jan 22, 2021	1) Severe illness (composite of ICU admission, mechanical ventilation, or mortality) n=241 (8.3%) 2) mortality n=167 (5.8%)	Admission	Inpatients RT-PCR+ within 5 days of admission (n = 2,892) 2 academic medical centers, 4 community hospitals Mass General Brigham Data Registry Enterprise Data Warehouse (Temporal validation)	Age, SpO2 Comorbidity (CCI)	N/A Logistic regression Survival analysis Right-censoring	Severe illness model: Age, SpO2, BUN, CRP, crea, low eGFR, eosinophils, ,glucose, LDH, lymphocytes, low ALC,monocytes, neutrophil, high ANC,plt, Trop T Charlson comorbidity index (CCI), prior respiratory infections Mortality model: Same as severe illness model plus low MCH ,high ANC, high absolute nucleated RBC , low plt PCT, RDW,Trop T, high WBC CCI, COPD or bronchiectasis, dementia or delirium external causes of injury lung CA respiratory failur e or insufficiency	severe illness: 0.79 (95% CI:0.75-0.81) mortality: 0.83 (95% CI:0.80-0.87)
Chua 2020 [24] UK	Prospective Multi- center March 1-May 16, 2020	In-hospital mortality TC, n=294 (29.9%)	Presentation to ED	Adults ≥18 years old PCR+ at Emergency Department (ED)	NEWS Demographic Routine laboratory tests	Usual data collected at the ED	SOARS11 SpO 2, obesity, age, RR, stroke, smoking,	SOARS11 TC 0.82 VC1 0.80 VC2 0.74

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
		(university hospital NHS Hospitals Trust) VC1 ISARIC n=4319 (30.35%) VC2 n= 94 (32.41%) (university hospital NHS Hospitals)		TC n=983 VC 1 n=14231 VC 2 n=290 n=5 confined at cut-off day			dementia, CKD with stage, Wbc count, lymphocytes CXR (≥4 zones affected) SOARS5: SpO2 , Obesity, Age, RR Stroke history	
Clift 2020 [9] UK	Retrospective	Time to death from COVID-19 TC n=4384 deaths (0.07%)# VC1: Jan 24- Apr 30, 2020 n=1722 (0.07%)# VC 2: May1- Jun 30,2020 n =621 (0.02%)# #% deaths in whole population (includes those with and without COVID-19	Not specified	Adults 19-100 years old QResearch database (1205 general practices in England linked to death and hospital registries TC n=6.08 million VC n= 2.17 million	Demographic data Comorbidity	Data available in the database	QCOVID Age Ethnicity Deprivation index BMI Comorbidity	Period 1 Women 0.93 (0.92, 0.94) Men0.93 (0.92, 0.93) Period 2 Women 0.95 (0.94, 0.96) Men0.93 (0.92, 0.95)
Cobos-Siles et al. 2020 CFS Spain	Retrospective	Mortality	Not specified	Inpatients RT PCR+ n=128	n/a	n/a	CFS	HR 8.73 (1.37-55.46)
Codon 2021 [25] CHADS CHA2DS2-VASc Spain	Retrospective Mar1- Apr 20, 2020	Thromboembolism n= 115 (3.78%) Mortality n=626 (20.58%)	Not stated i Presumed to be on admission	Inpatients confirmed COVID completed 1-month follow-up or died, Mar 1-Apr 20,2020	CHADS and CHA2DS2-VASc	–	CHADS CHF or LV ejection fraction ≤40, HPN, Age Stroke, transient ischaemic attack (TIA), systemic embolism	Thromboembolism CHADS 0.497 (0.452,0.542) CHA2DS2-VASc 0.490 (0.440,0.541) Mortality CHADS

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
							CHA2DS2-VASc score: age, sex, history of stroke, TIA, CHF, HPN, thromboembolism, diabetes mellitus	0.788 (0.770–0.807) CHA2DS2-VASc 0.794 (0.775,0.812)
Doganay 2021 CURB65 ISARIC-4C COVID-GRAM Turkey	Retrospective Kartal Dr. Lufti Kirdar City September 1 to December 2020	Mortality n=120 (24.94%) ICU requirement n = 85 (17.67%)	Admission	COVID-19 patients 18 and above RT PCR + n=481	n/a	n/a	Multiple models	Mortality CURB 65 0.846 (0.810-0.877) ISARIC 4C 0.784 (0.744-0.820) COVID GRAM 0.701 (0.658-0.742) ICU requirement CURB 65 0.898 (0.867-0.923) ISARIC 4C 0.797 (0.758-0.832) COVID-GRAM 0.684 (0.640-0.725)
Dres et al. 2021 CFS France Switzerland Belgium	Retrospective	Day-90 mortality n=549	Admission	Inpatients ICU RT PCR+ n=1199	n/a	n/a	CFS	Dres CFS 4 Univariate HR 2.14 (1.71-2.68) Multivariate HR 2.24 (1.63-3.09) CFS 5 Univariate 2.81 (2.17-3.64) Multivariate 2.83 (1.96-4.08)
El-Solh 2020 [26] US	Retrospective cohort Jan-May, 2020	In-hospital mortality n=475 (29.07%)	Admission	Inpatients RT-PCR+ n = 1634	–	–	Chen: Age, CHD, CVD, dyspnea, PCT, AST Shang: Age, CHD, %	Chen 14-day mortality: 0.67 (0.64–0.70) 21-day mortality: 0.68 (0.65–0.71)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
							lymphocytes, PCT, D-dimer Wang Clinical model: age, HPN, CHD Laboratory model: Age, hsCRP, peripheral capillary O2 sat, neutrophil and lymphocyte count, D-dimer, AST, GFR Yu: age, male sex, history of diabetes, lymphopenia, increased PCT	28-day mortality: 0.69 (0.66–0.72) Shang.: 0.72 (0.69–0.74) Yu: 0.63 (0.60, 0.66) Wang: 0.69 (0.66, 0.72)
Goodacre 2021 PRIEST UK	Retrospective March 26-May 29, 2022	Adverse outcome Derivation cohort n=11773 Validation cohort n=9118	Hospital admission	Adult COVID in patients DC 11773 VC 9118	Age, sex, RR, SBP, oxygen saturation, inspired oxygen, temperature, HR, NEWS2	LASSO regression	RR, O2 saturation, HR, SBP, Temp, Alertness, Inspired oxygen, Sex, Age, Performance status	DC 0.80 (0.79-.81) VC 0.83 (0.82-0.84)
Gupta 2020 [27] Multiple models 2(UK)	Retrospective Feb-Apr 2020	Mortality N=115 (28%) Clinical deterioration (ventilatory support or death) N=180 (43.8%	On hospital admission	Consecutive adults admitted to University College Hospital London, PCR+ or clinically diagnosed COVID-19 (diagnosis of ID Specialist - clinical features, laboratory, radiologic results without	n/a	n/a	22 models	Mortality Lu: 12-day 0.72 (0.67, 0.76) 30-day CURB-65: 0.74 (0.69, 0.79) BelloChavolla 0.66 (0.6, 0.72) In-hospital REMS: 0.76 (0.71, 0.81) qSOFA: 0.6 (0.54, 0.65) Xie: 0.76 (0.69, 0.82) Hu

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
				alternative diagnosis. n=411				0.74 (0.68, 0.79) Caramelo: 0.71 (0.66, 0.76) Zhang: 0.7 (0.65, 0.76) Yan: 0.58 (0.49, 0.67) Deterioration NEWS1 day 0.78 (0.73, 0.83) Ji: 10 days 0.56 (0.5, 0.62) Carr: 14 days 0.78 (0.74, 0.82) Guo: 0.67 (0.61, 0.73) Zhang: 0.74 (0.69, 0.79) Galloway: 0.72 (0.68, 0.77) TACTIC: 0.7 (0.65, 0.75) Colombi: 0.69 (0.63, 0.74) Huang: 0.67 (0.61, 0.73) Shi: 0.61 (0.56, 0.66) MEWS: 0.6 (0.56, 0.65)
Gupta , 2020 [14] UK	Prospective cohort Feb-Aug 2020	in-hospital clinical deterioration- initiation of ventilatory support (NIV, MV, ECMO); admission to ICU or death n = 31 924 (43.17%)	Admission or first clinical suspicion of covid	Inpatients Suspected/ Confirmed RT-PCR+ n = 73 948	Demographic, clinical, laboratory features, comorbidities	Review of iterature, availability in >60% of the study population	4C Deterioration Score: Age, sex + comorbidity + nosocomial infection + radiographic infiltrates + periph O2 sat + room air or o2, GCS, Urea, CRP, lymphocyte	0.77 (95% CI 0.76, 0.78)
Hewitt 2020	Retrospective cohort	In-hospital mortality	Admission	Inpatients RT PCR+ N=1564	n/a	n/a	CFS	CFS 1-2 HR 1

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
CFS UK Italy	Feb 27-April 28, 2020			Italy n=154 UK n=1410				3-4 HR 1.55 (1.00-2.41) 5-6 HR 1.83 (1.15-2.91) 7-9 2.39 (1.5-3.81)
Jung et al. CFS Germany	Prospective multicenter cohort March 19 to May 26 2020	survival status at 30 days after ICU admission (97%)	Admission	70 years and older with proven COVID-19 n=1346	n/a	n/a	CFS	Jung 3.20 (2.56-4.13) 2.41 (1.77-3.27) 1.86 (1.36-2.52)
King , 2021 [28] VACO USA	Retrospective Feb-July 2020	30-day mortality TC n=480 (13%) VC1 n=253 (12%) VC2 n=403 (5%)	Admission	Inpatients RT-PCR+ inpatients testing + within 14 days before or in the hospital (D1/ later)	DemographicComorbidity	Multivariable logistic regression	Age Sex Comorbidity MI or PVD	Hospital cohort: 0.80 (0.77, 0.83) Medicare cohort: 0.67 (0.67, 0.68) 0.68 (0.68 – 0.68)
Knight 2020 [12] 4C Mortality Score UK	Prospective cohort Feb-Jun 2020	Mortality TC n=11426 (32.22%) Feb 6-May 20, 2020 VC n=6729 (30.09%) May 21-June 29, 2020 No recorded outcome considered alive.	Hospital admission	Inpatients ≥ 18 years RT-PCR+ TC n= 35463 VC n= 22,361 (Temporal validation)	Patient and clinical variables Clinical biomarkers for COVID-19	41 candidate predictors selected a priori based on influence on outcome of pneumonia & flu-like illness, COVID-19, available for 2/3 of patients in TC 3-step model development	Age, sex, number of comorbidities R R, O2 sat, GCS, Urea,CRP	TC 0.786 (0.781,0.79) VC 0.767 (0.76, 0.773)
Li 2020 [29] PLANS China	Retrospective Jan-Mar 2020	In-hospital mortality TC n=211 (20.93%)	On admission	Inpatients Adults RT-PCR+	Patient characteristicLaboratory tests	Clinical knowledge, literature, data availability	Platelet count, lymphocyte cou nt,	TC 0.85 (0.83, 0.87) VC 0.87 (0.85, 0.89)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
		VC n=162 (15.71%)		TC (2 hospitals) Jan 1-Feb 10, 2020 n=1008 VC (1 hospital) Jan 14-Mar 8, 2020), n=1031		Multivariable Fine-Gray model	Age Neutrophil count Sex	
Liang 2020 COVID-GRAM China	Retropsective 575 hospitals in China January 2020	Critical illness defined as a composite measure of admission to the ICU, invasive ventilation, or death	admission	Inpatients Adults RT PCR + DC n=1590 VC n=710	72 variables including clinical signs and symptoms, imaging results, laboratory findings, demographic variables, and medical history	LASSO regression	X-ray abnormality, age, hemoptysis, dyspnea, unconsciousness, no. of comorbidities, cancer history, neutrophil to lymphocyte ratio, Lactate dehydrogenase U/L, direct bilirubin umol/L	DC 0.88 (0.84-0.93) VC 0.88 (0.84-0.93)
Liu FY 2020 [30] NEWS NEWS2REMS CURB- 65 qSOFA China	Retrospective Single- COVID center Jan 30-Mar 14, 2020	In-hospital death N=121 (17.98%)	On admission	Inpatients Adults RT-PCR+	n/a	n/a	NEWS NEWS2 REMS CURB-65 qSOFA	0.882 (0.847–0.916) 0.880 (0.845–0.914) 0.839 (0.800–0.879) 0.766 (0.718–0.814) 0.694 (0.641–0.746)
Liu H 2021 [31] PAWNN China	Retrospective Jan-Apr 2020	In-hospital death TC n=773 (7.88%) VC: China 211 (7.7%) Italian 77 (33.92%)	Admission and throughout hospitalization	Inpatients RT-PCR+ or clinically diagnosed Excluded leukemia inpatients at study end TC n=9810 VC1 n=2739 VC2 n=227	38 candidate predictors Demographic Clinical findings Laboratory tests-CBC	Generalized linear mixed modelling, Cox regression model	Platelet count Age WBC count Neutrophil count Neutrophil:lymphocyte ratio	TC 0.92-93 (0.91, 0.94) VC Chinese 0.97 (0.96–0.98) Italian 0.80 (0.74, 0.86)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
Mancilla-Galindo, 2021 [32] Mexico	Retrospective	Mortality TC n=9228 (11.01%) VC n=5278 (5.28%)	Not mentioned	Inpatients Ambulatory RT-PCR+ TC n=83779 VC n=100,000	Demographic, Clinical Comorbidity	Demographic Patient history predictors for low-resource settings Univariate and multivariate regression	Age Sex Diabetes COPD Immunosuppression Hypertension Obesity CKD	0.8 (0.796, 0.804)
Marcolino 2021 [13] ABC$_2$-SPH Brazil	Retrospective Mar-Jul 2020. Aug-Sep 2020	In-hospital deaths TC n=806 (20.26%) VC1 Brazil n=208 (19.73%) VC2 Spain 82 (17.29%)	Admission	Inpatients PCR+ TC n=3978 VC1 n=1054 VC2 n=474	20 predictors chosen a priori Demographic Comorbidity Vital signs Laboratory tests	Least absolute shrinkage and selection operator (LASSO) logistic regression	Age, blood urea nitrogen, number of comorbidities, HR, CRP, SpO2/FiO2 ratio, platelet count	TC 0.844 (0.829,0.859) VC1 0.859 (0.833, 0.885) VC2 0.899 (0.864,0.934)
Miles et al. CFS UK	prospective May 2020	all-cause mortality n=217	Admission	Inpatients RT-PCR+ n=217 COVID-19 cases	n/a	n/a	CFS	Miles CFS Univariate HR 1.12 (1..02-1.23) Multivariate HR 1.88 (1.37-2.59) CFS x COVID-19 Multivariate HR 0.51 (0.27-0.71)
Nafilyan 2021 [10] QCOVID England	Retrospective Jan-July 2020	Suspected/ confirmed COVID-related death (ICD code) n=26,985 (0.077 %)[a] deaths in Period 1 (Jan 24-Apr 30, 2020) n=13,177 (0.037%)[a] in Period 2 (May1-Jul 28, 2020)	No particular time	Adults n=34.897M (ONS PH Health Linked Data Asset linked to primary care and hospital databases) Patients entered the COVID cohort on Jan 24 & follow-up till Jul 28,2020	Demographic data Comorbidity	n/a	QCOVID Age, Sex Region Ethnicity Townsend deprivation scale Accommodation BMI Comorbidity (CKD, Cancer, Chemotherapy, Immunosuppression, Learning Disability Others)	C statistic Period 1 Men 0.935 (0.933, 0.937) Women 0.945 (0.943, 0.947) Period 2 Men 0.944 (0.942, 0.946) Women 0.956 (0.954, 0.958)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
		-% deaths in whole population (includes those with and without COVID-19						
Nava 2020 [33] US	Retrospective Teaching community hospital Mar-May 2020	In-hospital mortality n=101 (32.26%) ICU admission n=98 (31.3%)		Inpatients adults COVID-19 pneumonia n=313			CURB-65 Quick COVID-19 Severity Index (qCSI) Brescia - COVID Respiratory Severity Scale (BCRSS)	CURB-65 0.781 qCSI score 0.711 BCRSS prediction rule 0.663
Nicholson 2021 [34] VICE DICE US	Retrospective Metropolitan hospital network until May 19, 2020	Death TC n=111 (19.2%) VC n=99 (21.33%) Mechanical Ventilation TC n=243 (42.04%) VC n=161 (34.69%	On admission Laboratory tests within 24 hours of admission (Research Patient Data Repository)	Inpatients Adults RT-PCR+ Observed until discharge TC n=1042 VC1= 578 (1 hospital) VC2 n= 464 (4 hospitals)	Demographic, clinical, and admission laboratory data	Multivariate logistic regression analysis with backwards selection stepwise method	DICE: Age, male sex, CAD, DM, chronic statin use, SpO2:FiO2 ratio,BMI, NLR, platelet count, procalcitonin VICE: DM SpO2:FiO2 ratio, CRP, LDH	DICE TC 0.91 (0.87,0.94) VC 0.79 (0.74,0.84) VICE TC 0.84 (0.80,0.87) VC 0.86 (0.82,0.90)
Neto 2021 [ ] CURB CURB 65 QSOFA PSI SMART COP IDSA/ATS Minor REA-ICU SCAP COVID GRAM CALL 4C	Binational retrospective cohort Hospital das Clinicas in Sao Paulo, Brazil Hospital Clinic Barcelona	In hospital mortality 30 days n=320 (23.48%), Brazil n=228 (24.65), Spain n=92 (21%) ICU admission n=646 (47.4%), Brazil n=487 (52.65%), Spain n=159 (36.3%)	On the first medical assessment in the emergency department and laboratory tests were taken from the first available result up to 48 h after admission	Adult in-patients (Barcelona – RT PCR + only, Sao Paulo, RT PCR + and clinical-epidemiologically diagnosed) All N=1363 Brazil n=925, Spain n=438	n/a	n/a	Multiple models	30-day in-hospital mortality CURB 0.71 (0.68-0.74) CURB65 0.74 (0.72-0.77) QSOFA 0.63 (0.6-0.66) PSI 0.79 (0.77-0.82) SMART COP (0.71 (0.68-0.74) IDSA/ATS Minor 0.73 (0.7-0.76)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
Brazil Spain								REA-ICU 0.69 (0.65-0.72) SCAP 0.74 (0.71-0.77) COVID GRAM 0.77 (0.75-0.8) CALL 0.71 (0.68-0.74) 4C 0.78 (0.75-0.81) 7-day ICU admission CURB 0.59 (0.55-0.62) CURB65 0.54 (0.51-0.58) QSOFA 0.59 (0.56-0.62) PSI 0.52 (0.49-0.56) SMART COP (0.64 (0.61-0.67) IDSA/ATS Minor 0.6 (0.57-0.64) REA-ICU 0.6 (0.67-0.63) SCAP 0.6 (0.57-0.63) COVID GRAM 0.52 (0.48-0.55) CALL 0.52 (0.49-0.56) 4C 0.55 (0.52-0.59)
Paranjape 2021 [35] Calculator for ICU transfer US	Retrospective Large metropolitan health system Mar-Jul 2020	Transfer to ICU service TC n=804 (39.92%) VC n= 192 (28,61%)	On admission	Inpatients Adults RT-PCR+, TC Mar-Jul n=2014 VC: July n=671	Demographic (age, sex, race, BMI), temp, SpO2 on room air CRP, LDH, ferritin, D dimer, absolute lymphocyte count	Multivariate Logistic Regression analysis with backwards selection stepwise method	DM, CAD, CKD, CRP, LDH	TC 0.752 VC 0.769

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
					Comorbidities- HTN, DM CKD,Asthma, COPD, CAD			
Richardson 2021 [36] NEWS2/NEWS UK	Retrospective	Death 24 hrs-9 48 hrs-15 72 hrs-33 In-hospital- 199 (32.09%)	Within 24 hours of admission	Adults non-elective admission (COVID or not) discharged Mar11-Jun 13, 2020 COVID as ICD-coded in EMR	n/a	n/a	NEWS: RR, HR, temp, O2Sat, O2 supplement, AVPU, SBP NEWS2 NEWS and alertness includes confusion	NEWS 0.64 NEWS2 0.64 72hours NEWS: 0.75 NEWS2: 0.71 48 hours NEWS: 0.78 NEWS2: 0.76 24hours NEWS: 0.84 NEWS2: 0.86
Schoning 2021 [37] COSA Switzerland	Retrospective Prospective validation Feb-Nov 2020	Severe TC n=63 (31.82%) VC n=105 (22.87%)	On admission Lab values 3 days before or up to 1 day after PCR+	In- and outpatients 198 PCR+ TC n=198 Feb-Aug VC n=459 Sep-Nov	Medical history, demographicsTop 20 laboratory tests routinely assessed on admission	Logistic regression Repeated cross-validation	COSA score Sex CRP Sodium Hemoglobin eGFR Glucose Leukocyte count	TC 0.94 (0.87, 0.95) VC 0.85
Solem 2021 [11] COPE Denmark	Prospective cohort 2 regions Denmark Mar 1 to June 16, 2020	TC Hospital admission n=1359 (34.5%) ICU n=181 (4.6%) Death n=324 (8.2% of COVID-19 patients or 0.01% of whole population tested)	Different time points: Diagnosis First 12 h of hospital admission 12 hours prior to ICU admission -12 hours after ICU admission	Adults at PCR test (Regional EMR with in-hospital data) 3944 RT-PCR+ out of 2.6M tested TC Denmark VC: UK Biobank n=1650	Demographic data Comorbidity Temporal features In-hospital laboratory tests	Available information in the EMR Random forests Cross-validation	Base model-Age, sex, BMI Model 2: Base +comorbidity Model 3: Model 2+temporal features Model 4: Model 3+in-hospital laboratory tests	TC: Risk of death 0.906 at diagnosis, 0.818, at admission 0.721 at ICU admission ICU admission On diagnosis, Model 2,3 &4 with improved prediction On

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
		VC Hospitalized n=753 (45.63%) ICU n=131 (17.4%) Deaths n=305 (18.48%)						admission Model 4 significantly improves prediction VC On Diagnosis Mortality 0.742 ICU admission 0.529 Hospital admission 0.661
Tanboga 2021 [38] CORONATION TURKEY	Retrospective National database Mar-Jun 2020	Total deaths n=2682 (4.4%) ICU n=7688 (13%) Mechanical ventilation n=4867 (8%) 30-day death TC n=2343 (6%) VC n=339 (2%) ICU TC n=6160 (15%) VC n=1528 (8%) Mechanical ventilation TC n=4158 (10%) VC n=709 (4%)	Admission	Inpatient RT-PCR+ n=60,980 TC n=41,300 VC n=19,6809	Demographic data ComorbiditiesLung CT Laboratory tests	Data from public health management system for COVID-19 specific data during index hospitalization (symptoms, biomarkers, medication, comorbidity, clinical outcomes)	Age, findings from lung CT, LDH, CRP, comorbidities, NLR, and D-dimer	Temporal validation TC 0.933 (0.929–0.937) VC 0.956 (0.948–0.964) Geographic validation Istanbul TC Istanbul 0.958 (0.939–0.972) VC: Anatolia region 0.896 (0.890–0.902)
Van Dam 2020 [39] Netherlands	Retrospective study ED of a single secondary/ tertiary hospital Mar-May 2020	30-day mortality N=95/403 (23.57%)	On admission	Adults on ED consult RT-PCR+ or clinical diagnosis (symptom, CT findings with consent) n=403 307were admitted	n/a	n/a	RISE-UP CURB-65 MEWS REMS abbMEDS SOFA APACHE II	30-day mortality 0.83 (0.79-0.88) 0.75 (0.70-0.80) 0.64 (0.58-0.70) 0.73(0.68-0.78) 0.75(0.70-0.81) 0.72(0.67-0.78) 0.71(0.65-0.78)

Author and year Model	Study design and Setting	Specific Outcome	Time point of model application	Population and sample size	Candidate predictors	Determination of candidate predictors	Final predictors	Performance AUC (95% CI)
Van Dam 2021[40] RISE UP Netherlands	Retrospective 2 EDs Mar-May 2020	30-day mortality n=167 (26%) Composite of 30-day mortality,ICU ICU n=102 (15.9%)	During Emergency Department Visit	Adults on ED visits RT-PCR+ or clinically diagnosed (sym ptom, CT finding)			RISE-UP score Age, abnormal vital signs (any of HR, MAP, RR, O2Sat, temp, GCS) serum albumin BUN, LDH, bilirubin with or without O2 supplement	Mortality 0.77 (0.73, 0.81) Composite 0.72 (0.68,0.76)
Van Klaveren 2021 [41] COPE Netherlands	Retrospective 4 hospitals Mar-Aug 2020	326 deaths (10.02%)	Admission to hospital	Admitted from ED suspected COVID 19 n=3252 Temporal validation	Patient characteristics (sex, age, BMI) Vital statistics Laboratory tests	Literature review Available at ED setting Logistic regression with post-hoc uniform shrinkage	Age, RR, CRP, LDH, alb, urea	AUC in 4 hospitals: 0.82 [0.78; 0.86] 0.82[0.74; 0.90] 0.79 [0.70;0.88] 0.83 [0.79; 0.86]

AUC = Area Under the Curve; VC=Validation cohort; TC=Training cohort

Appendix 3. Clinical appraisal of included studies using the PROBAST tool

Study	ROB				Applicability			Overall judgment	
	Participants	Predictors	Outcome	Analysis	Participants	Predictors	Outcome	ROB	Applicability
Adderley et al.	L	L	L	H	U	U	L	**H**	**U**
Ageno et al.	L	L	L	H	U	U	L	**H**	**U**
Artero et al.	H	U	L	H	U	U	L	**H**	**U**
Baker et al.	H	L	H	H	U	L	L	**H**	**U**
Bartoletti et al.	H	L	H	H	U	U	L	**H**	**U**
Berenguer et al.	L	L	L	H	U	U	L	**H**	**U**
Bradley et al.	H	L	H	U	U	U	L	**H**	**U**
Carr et al.	L	L	L	H	L	U	U	**H**	**U**
Castro et al.	L	L	L	H	U	U	L	**H**	**U**
Chua	H	H	U	U	U	U	L	**H**	**U**
Clift et al.	L	L	L	L	U	U	L	**L**	**U**
Codon	H	U	U	H	U	U	L	**H**	**U**
El Sohl et a.	H	L	L	H	U	U	L	**H**	**U**
Gupta 2020	H	L	L	U	U	U	L	**H**	**U**
Gupta 2021 4C	L	U	L	L	U	U	L	**U**	**U**
King et al.	L	L	L	H	L	U	L	**H**	**U**
Knight	L	L	L	U	U	U	L	**U**	**U**
Li J	H	U	H	L	U	U	L	**H**	**U**
Liu FY	H	L	L	H	U	U	L	**H**	**U**
Liu H	L	L	U	H	U	U	L	**H**	**U**
Mancilla-Galindo	H	L	L	H	L	U	L	**H**	**U**
Marcolino	L	L	L	U	U	U	L	**U**	**U**
Nafilyan	L	L	L	L	U	U	L	**L**	**U**
Nava	U	U	H	H	U	U	L	**H**	**U**
Nicholson	L	U	L	H	U	U	L	**H**	**U**
Paranjape	L	U	U	H	U	U	L	**H**	**U**
Richadson	L	L	L	H	U	U	L	**H**	**U**
Schoning	U	U	L	H	U	U	L	**H**	**U**
Solem	L	L	L	U	U	U	L	**U**	**U**

Study	ROB				Applicability			Overall judgment	
	Participants	Predictors	Outcome	Analysis	Participants	Predictors	Outcome	ROB	Applicability
Tanboga	U	U	H	H	U	U	L	**H**	**U**
van Dam RISE UP	L	U	L	H	U	U	L	**H**	**U**
van Dam	L	L	L	H	U	U	L	**H**	**U**
van Klaveren	U	H	U	H	U	U	L	**H**	**U**
Liang 2020	U	U	L	H	L	L	U	**H**	**U**
Armiñanzas 2021	L	U	L	H	L	L	U	**H**	**U**
Neto 2021	L	U	L	L	L	L	L	**U**	**L**
Doganay 2021	L	U	L	H	L	L	L	**H**	**L**
Aliberti 2021	L	U	L	H	L	L	L	**H**	**L**
Apea 2020	U	U	L	H	L	L	L	**H**	**L**
Aw 2020	L	U	L	U	L	L	L	**U**	**L**
Cobos-Siles 2020	U	L	L	U	L	L	L	**U**	**L**
Dres 2021	U	U	L	U	L	L	L	**U**	**L**
Hewitt 2020	L	U	L	H	L	L	L	**H**	**L**
Jung 2021	H	H	L	U	U	L	L	**H**	**U**
Miles 2020	L	U	L	H	L	L	L	**H**	**L**
Thompson 2021	U	U	L	U	L	L	L	**U**	**L**

Appendix 4. GRADE Evidence Profile

Author(s): Patricia Pauline Remalante-Rayco, Evelyn Salido
Question: Prognostic models compared to no prognostic models for prediction of worsening severity/clinical deterioration/poor outcomes and mortality in adults with COVID-19
Setting:
Bibliography:

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
QCOVID									
2	observational studies	not serious	not serious	not serious	not serious	very strong association		⨁⨁⨁⨁ HIGH	
4C Deterioration Score									
1	observational studies	not serious	not serious	not serious	not serious	none		⨁⨁◯◯ LOW	
COPE									
1	observational studies	serious [a]	not serious	not serious	not serious	none		⨁◯◯◯ VERY LOW	
ABC2-SPH									
1	observational studies	serious [b]	not serious	not serious	not serious	strong association		⨁⨁◯◯ LOW	
4C Mortality Score									
2	observational studies	serious [b]	not serious	not serious	not serious	none		⨁◯◯◯ VERY LOW	
CURB-65									
5	observational studies	serious [c,d,e]	not serious	not serious	not serious	strong association		⨁⨁◯◯ LOW	
REMS									
3	observational studies	serious [c,e]	not serious	not serious	not serious	strong association		⨁⨁◯◯ LOW	
RISE-UP									
2	observational studies	serious [c,d,e]	not serious	not serious	not serious	strong association		⨁⨁◯◯ LOW	
qSOFA									
4	observational studies	serious [c,e]	not serious	not serious	not serious	none		⨁◯◯◯ VERY LOW	
MEWS									
2	observational studies	serious [e]	not serious	not serious	not serious	none		⨁◯◯◯ VERY LOW	
NEWS2									
5	observational studies	serious [c,d,e,f]	serious [g]	not serious	not serious	none		⨁◯◯◯ VERY LOW	

CI: Confidence interval

Explanations

a. Did not account for censoring
b. Continuous predictors were dichotomized
c. Exclusion of participants with missing data
d. Calibration not done
e. Complexities in data not addressed
f. Small number of events relative to number of predictors
g. Outlier study (1 study with higher AUC)

Appendix 5. Characteristics of Ongoing Studies

Study name	Methods	Participants	Interventions	Outcomes	Starting date	Notes
NCT04366024 A Novel Nomogram to Predict Severity of COVID-19	Retrospective observational study (case-only)	COVID-19 disease patients confirmed by virus nucleic acid RT-PCR and CT	clinical diagnosis	Consistency of predicted severe rate and observed severe rate of COVID-19 patients (Time frame: up to 3 months) Duration of severe illness (Time frame: up to 3 months)	January 17, 2020	recruiting
NCT04629183 Risk Stratification of COVID-19 Patients Discharged From the Emergency Department (CODED)	Prospective cohort study	Adult patients (>18 years) subjected to a first ED visit for physician-confirmed COVID-19, discharged from the ED based on attending physician's or patient's decision (independent from study participation)	integrated clinical evaluation	Primary: Composite outcome of death (any cause), hospital admission (any cause) (Time Frame: up to 30 days) Secondary: Death from COVID-19; death from other disease; hospital admission for COVID-19; hospital admission for other disease (Time Frame for all secondary outcomes: 30 days)	November 1, 2020	Recruiting