Article

ABC2-SPH risk score for in-hospital mortality in COVID-19 patients: development, external validation and comparison with other available scores

Supplementary material

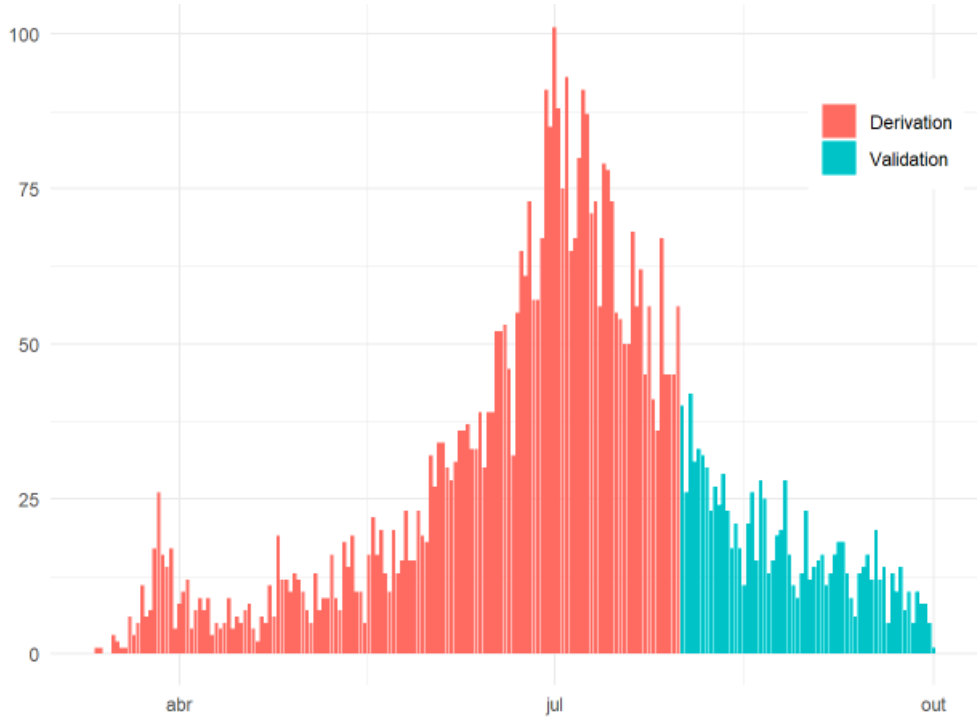


Figure S1. Graphical representation of development and validation cohorts

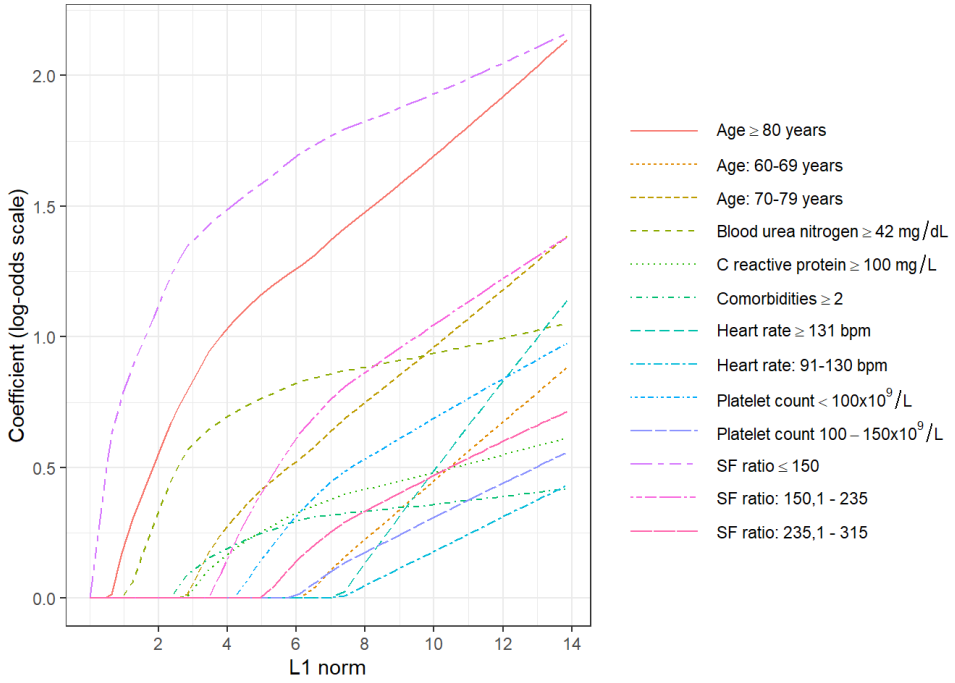
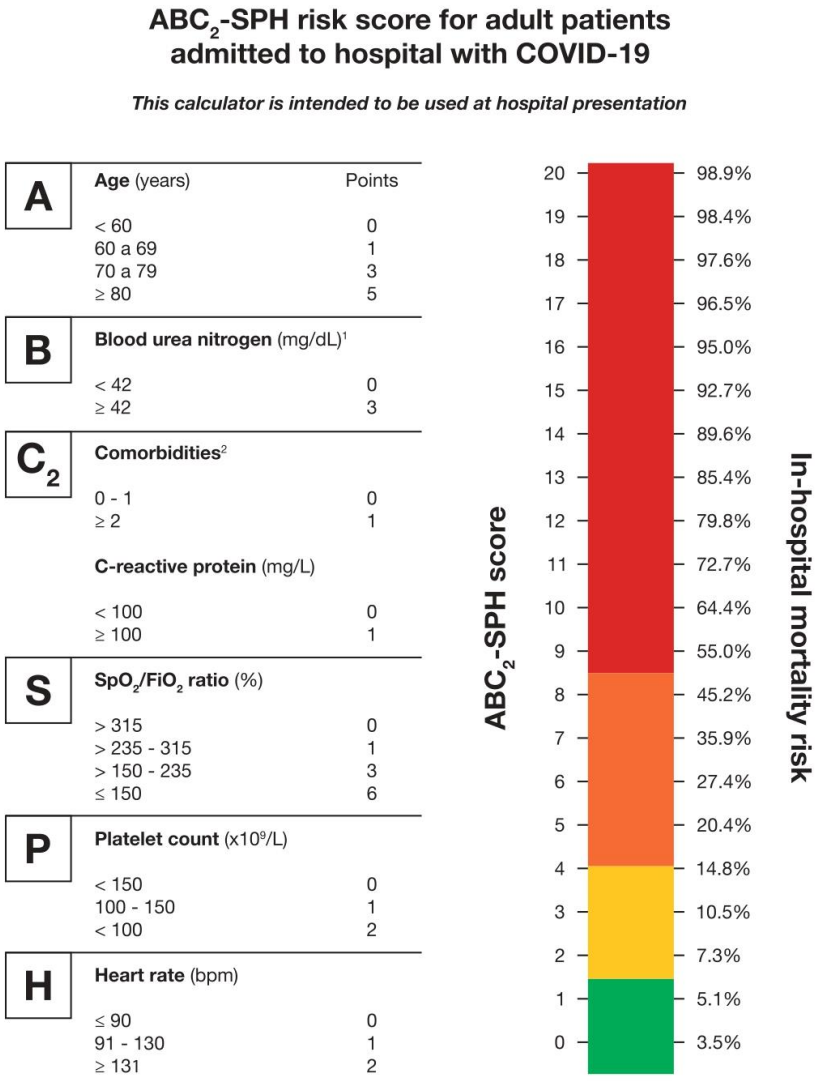


Figure S2. Least absolute shrinkage and selection operator logistic regression (LASSO) trace plot

Figure S3. ABC_2-SPH score infographics in English, Portuguese and Spanish



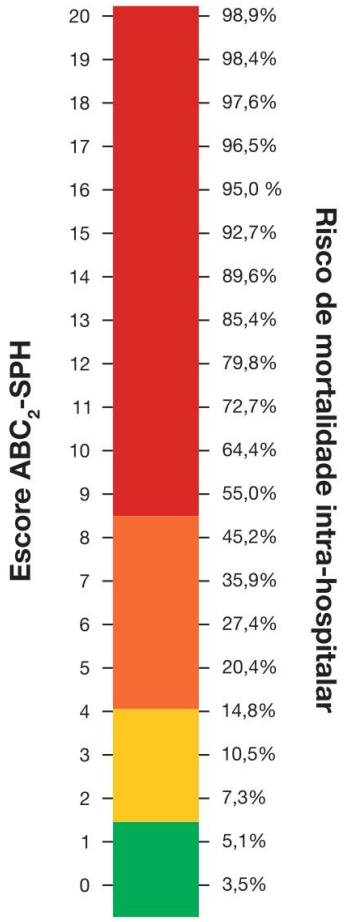
1. When converted to urea, the cut-off is 90 mg/dL.
2. Hypertension, coronary artery disease, heart failure, atrial fibrillation or flutter, stroke, COPD, diabetes mellitus, obesity (BMI > 30 kg/m²), cirrhosis and cancer.

Marcolino MS, Pires MC, Ramos LEF, Silva RT, Oliveira LM et al. ABC_2-SPH risk score for in-hospital mortality in COVID-19 patients: development, external validation and comparison with other available scores. MedRxiv 2021.02.01.21250306.

Escore ABC_2-SPH para pacientes adultos admitidos no hospital com COVID-19

Este escore deve ser usado na admissão hospitalar

A	**Idade** (anos)	Pontos
	< 60	0
	60 a 69	1
	70 a 79	3
	≥ 80	5
B	**Ureia** (mg/dL)	
	< 90	0
	≥ 90	3
C_2	**Comorbidades**[1]	
	0 - 1	0
	≥ 2	1
	Proteína C-reativa (mg/L)	
	< 100	0
	≥ 100	1
S	**Relaçao SpO_2/FiO_2** (%)	
	> 315	0
	> 235 - 315	1
	> 150 - 235	3
	≤ 150	6
P	**Contagem de plaquetas** (/mm^3)	
	< 150.000	0
	100.000 - 150.000	1
	< 100.000	2
H	**Frequência cardíaca** (bpm)	
	≤ 90	0
	91 - 130	1
	≥ 131t	2



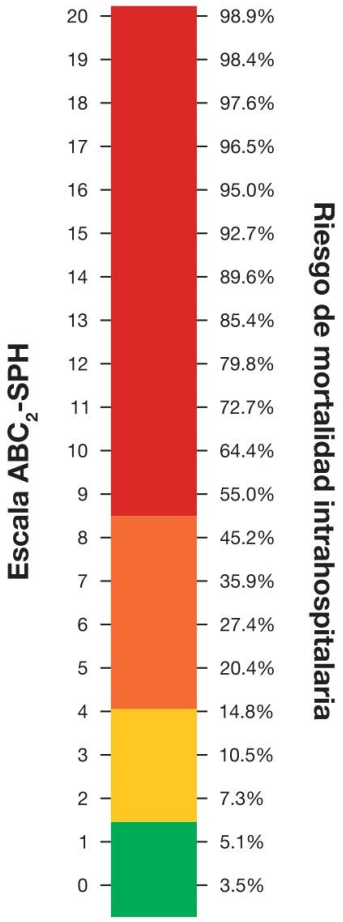
1. Hipertensão arterial, doença arterial coronariana, insuficiência cardíaca, fibrilação atrial ou flutter, acidente vascular cerebral, DPOC, diabetes mellitus, obesidade (IMC > 30 kg/m^2), cirrose e câncer.

Marcolino MS, Pires MC, Ramos LEF, Silva RT, Oliveira LM et al. ABC_2-SPH risk score for in-hospital mortality in COVID-19 patients: development, external validation and comparison with other available scores. MedRxiv 2021.02.01.21250306.

Escala de riesgo ABC2-SPH para pacientes adultos ingresados en el hospital por COVID19

Esta calculadora está diseñada para ser usada en el primer contacto del paciente con el hospital

A	**Edad** (años)	Puntos
	< 60	0
	60 a 69	1
	70 a 79	3
	≥ 80	5
B	**Nitrógeno ureico en sangre** (mg/dL)[1]	
	< 42	0
	≥ 42	3
C_2	**Comorbilidades**[2]	
	0 - 1	0
	≥ 2	1
	Proteína C-reactiva (mg/L)	
	< 100	0
	≥ 100	1
S	**Razón SpO_2/FiO_2** (%)	
	> 315	0
	> 235 - 315	1
	> 150 - 235	3
	≤ 150	6
P	**Recuento de plaquetas** (/mm^3)	
	< 150.000	0
	100.000 - 150.000	1
	< 100.000	2
H	**Frecuencia cardíaca** (lpm)	
	≤ 90	0
	91 - 130	1
	≥ 131	2



1. Si se utiliza urea el punto de corte es 90 mg/dL.
2. Hipertensión arterial, cardiopatía isquémica, insuficiencia cardíaca, fibrilación auricular o flutter, enfermedad cerebrovascular, EPOC, diabetes mellitus, obesidad (IMC > 30 kg/m^2), cirrosis y cáncer.

Marcolino MS, Pires MC, Ramos LEF, Silva RT, Oliveira LM et al. ABC_2-SPH risk score for in-hospital mortality in COVID-19 patients: development, external validation and comparison with other available scores. MedRxiv 2021.02.01.21250306.

(a) (b)

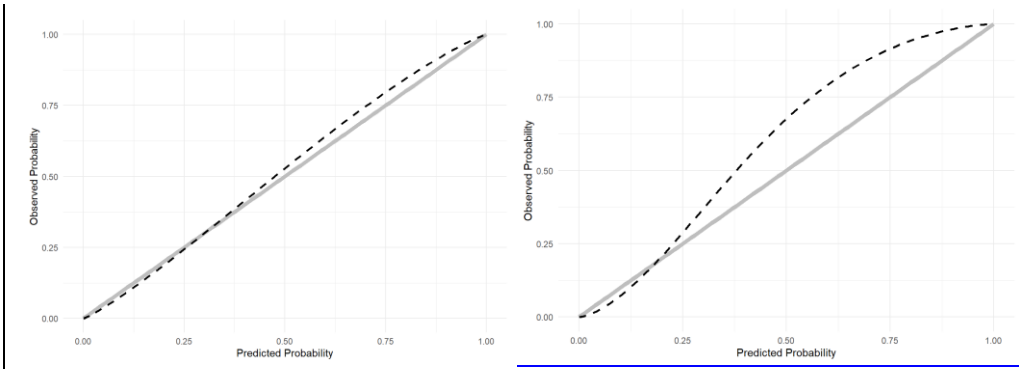


Figure S4. Calibration plot of ABC_2-SPH Score in (a) Brazilian and (b) Spanish external validation cohorts

Table S1. Demographic and clinical characteristics for patients admitted to hospital with COVID-19 and were transferred to other hospitals (n=77)

Characteristic	Frequency (%) or median (IQR)	Non missing cases (%)
Age (years)	55.0 (51.0, 70.0)	77 (100%)
Sex at birth		77 (100%)
Male	48 (62.3%)	
Comorbities		
Hypertension	41 (53.2%)	77 (100%)
Coronary artery disease	4 (5.2%)	77 (100%)
Heart failure	5 (6.5%)	77 (100%)
Atrial fibrillation or flutter	2 (2.6%)	77 (100%)
Stroke	3 (3.9%)	77 (100%)
COPD	4 (5.2%)	77 (100%)
Diabetes mellitus	22 (28.6%)	77 (100%)
Obesity (BMI>30kg/m^2)	8 (10.4%)	77 (100%)
Cirrhosis	2 (2.6%)	77 (100%)
Cancer	5 (6.5%)	77 (100%)
Number of comorbidities		77 (100%)
0	23 (29.9%)	
1	24 (31.2%)	
2	20 (26.0%)	
3	8 (10.4%)	
4	2 (2.6%)	
Clinical assessment at admission		
SF ratio	433.3 (350.0, 447.6)	75 (97.4%)
Respiratory rate (irpm)	22.0 (18.0, 24.0)	61 (79.2%)
Heart rate (bpm)	89.0 (78.2, 99.8)	70 (90.9%)
Glasgow coma score	15.0 (15.0, 15.0)	75 (97.4%)
Systolic blood pressure (mmHg)		70 (90.9%)
< 90	2 (2.9%)	
≥ 90	68 (97.1%)	
Diastolic blood pressure(mmHg)		70 (90.9%)
≤ 60	12 (17.1%)	
> 60	58 (82.9%)	
Inotrope need at admission	0 (0%)	
Laboratory		
Hemoglobin (g/L)	13.6 (12.2, 14.9)	71 (92.2%)
Platelet count (10^9/L)	196.0 (144.0, 250.0)	71 (92.2%)
Neutrophils-to-lymphocytes ratio	5.7 (4.0, 8.4)	62 (80.6%)
Lactate (mmol/L)	1.3 (1.1, 1.9)	45 (58.4%)
C-reactive protein (mg/L)	87.5 (61.2, 134.5)	62 (80.6%)
BUN (mg/dL)	41.0 (19.1, 28.5)	69 (89.6%)
Creatinine (mg/dL)	1.1 (0.8, 1.4)	73 (94.8%)
Sodium (mmol/L)	138.0 (135.0, 141.0)	65 (84.4%)
Bicarbonate (mEq/L)	21.9 (20.0, 23.2)	59 (76.6%)
pH	7.4 (7.4, 7.5)	60 (77.9%)
pO2 (mmHg)	78.0 (62.1, 99.7)	59 (76.6%)
pCO2 (mmHg)	32.0 (27.9, 35.5)	59 (76.6%)

BMI: body mass index; BUN: blood urea nitrogen; COPD: chronic obstructive pulmonar disease; SF ratio: SpO_2/FiO_2 ratio.

Table S2. Assessment of potential predictors for the model development

Variables	Scientific evidence	Model development (derivation cohort)
Demographics characteristics		
Sex at birth	Halalau *et. al*[68]; 4C Mortality Score[36]; VICE and DICE[51]; COVID-19 Inpatient Risk Calculator (CIRC)[73]; Kazemi *et.al*[75]; Altschul *et. al*[65]; Galloway *et. al*[69]; DCS, DCSL and DL[38]; 17F[80]; CARMc19_N and CARMc19_NB[81]; COVER-F for death[86]; COVID-19 Mortality Socre[87]; CoCoMoRP[88]; Sarkar and Chakrabarti[90].	Included as candidate predictor
Age (years)	A-DROP[91]; Halalau *et. al*[68]; COVID-19MRS[10]; 4C Mortality Score[36]; COVID-GRAM[41]; VICE and DICE[51]; COVID-19 Inpatient Risk Calculator (CIRC)[73]; Sourij *et. al*[74]; Kazemi *et.al*[75]; Núñez-Gil *et. al*[76]; Allenbach *et. al*[14]; Altschul *et. al*[65]; COVID-AID[44]; FAD-85[13]; COVEB[77]; Galloway *et. al*[69]; Bello-Chavolla *et. al*[78]; ANDC[52]; Xie *et.al*[37]; Yoo *et. al*[79]; DCS, DCSL and DL[38]; 17F and 3F models[80]; CSS score[54]; CARMc19_N and CARMc19_NB[81]; Mei *et. al*[82]; Zhang *et. al*[8]; ACP risk grade[83]; LOW-HARM[84]; COVER-F for death[86]; COVID-19 Mortality Socre[87]; CoCoMoRP[88]; NOCOS Calculator[59]; Chen *et. al*[89]; Sarkar and Chakrabarti[90]; Hu *et. al*[55].	Included as candidate predictor
Ethnicity	17F[80]; Galloway *et.* al[69].	Not recorded within database
Hypertension	Halalau *et. al*[68]; COVID-19MRS[10]; Núñez-Gil *et. al*[76]; Galloway *et. al*[69]; Bello-Chavolla *et. al*[78]; DCS[38]; LOW-HARM[84]; COVER-F for death[86]; COVID-19 Mortality Socre[87].	Combined with other comorbities
Coronary artery disease	Halalau *et. al*[68]; COVID-GRAM[41]; CSS score[54]; COVID-19 Mortality Socre[87]; Chen *et. al*[89].	Combined with other comorbities
Heart failure	Halalau *et. al*[68]; Kim *et. al*[15]; COVID-19	Combined with other comorbities

	Mortality Socre[87].	
Atrial fibrillation or flutter	Kim *et. al*[15]; COVID-19 Mortality Socre[87].	Combined with other comorbities
Stroke	Charlson Comorbidity Index[35]; COVID-GRAM[41].	Combined with other comorbities
COPD	COVID-GRAM[41]; Bello-Chavolla *et. al*[78]; 17F[80]; COVER-F for death[86].	Combined with other comorbities
Diabetes mellitus	VICE and DICE[51].	Combined with other comorbities
Obesity (BMI>30kg/m^2)	Halalau *et. al*[68]; 17F[80]; Núñez-Gil *et. al*[76]; Bello-Chavolla *et. al*[78].	Combined with other comorbities
Cirrhosis	Charlson Comorbidity Index[35], 4C Mortality Score[36].	Combined with other comorbities
Cancer	COVID-19MRS[10]; COVID-GRAM[41]; DCS and DCSL[38]; 17F[80]; COVER-F for death[86].	Combined with other comorbities
Smoking	Salah, Sharma and Mehta[92].	High collinearity with COPD, not included
Number of comorbidities	COVID-19MRS[10]; 4C Mortality Score[36]; COVID-GRAM[41].	Included as candidate predictor
Clinical characteristics		
Respiratory rate (irpm)	COVID-19MRS[10]; 4C Mortality Score[36]; Gavelli *et. al*[67]; Galloway *et.* al[69].	Included as candidate predictor
Heart rate (bpm)	NEWS2[93].	Included as candidate predictor
Systolic blood pressure (mm Hg)	CURB65[29].	Combined with inotrope requirement and included as candidate predictor
Diastolic blood pressure (mm Hg)	17F[80]; CURB65[29].	High collinearity with systolic blood pressure, not included
Inotrope use	SOFA[94].	Combined with systolic and diastolic blood pressure
Glasgow coma score	Yoo *et. al*[79].	Included as candidate predictor
Temperature (ºC)	17F[80]; Mei *et. al*[82].	Too many missing values, not included
SF ratio	Choi, Hong and Kim[95]; Choi *et. al*[95].	Included as candidate predictor predictor
Laboratory		
Mechanical ventilation	Lim *et. al*[96].	Included as candidate predictor
C reactive protein (mg/L)	VICE and DICE[51]; ANDC[52].	Included as candidate predictor
Hemoglobin (g/L)	Lippi and Mattiuzzi[97].	Included as candidate predictor

Neutrophils-to-lymphocytes ratio	COVID-GRAM[41]; ANDC[52]; VICE and DICE[51].	Included as candidate predictor
Platelet count (10^9/L)	SOFA[94]; VICE and DICE[51]; EDRnet[58]; COVID-19 Mortality Socre[87].	Included as candidate predictor
Creatinine (mg/dL)	COVID-19MRS[10]; COVID-AID[44]; Altschul *et. al*[65]; Galloway *et.* al[69]; DCSL and DL[38]; LOW-HARM[84]; SOFA[94].	Included as candidate predictor
Urea (mg/dL)	4C Mortality Score[36]; EDRnet[58]; NOCOS Calculator[59], CURB65[29].	Included as candidate predictor
Lactate (mmol/L)	COVID-GRAM[41]; NLAUD[16]; Xie *et.al*[37].	Included as candidate predictor
Sodium (mmol/L)	PSI[98].	Included as candidate predictor
Bicarbonate (mEq/L)	EDRnet[58].	Included as candidate predictor
pH	Li *et. al*[99].	Included as candidate predictor
pO2 (mmHg)	SOFA[94].	Included as candidate predictor
pCO2 (mmHg)	Li *et. al*[99].	Included as candidate predictor
Ferritin (mcg/L)	FAD-85[13].	Too many missing values, not included
NT-proBNP (pg/mL)	Kim *et. al*[15].	Too many missing values, not included
Creatine kinase (U/L)	Kim *et. al*[15].	Too many missing values, not included
Troponin (ng/mL)	Yoo *et. al*[79].	Too many missing values, not included
Bilirubin (mg/dL)	SOFA[94]; COVID-GRAM[41]; Zhang *et. al*[8]; Chen *et. al*[89].	Too many missing values, not included
Partial thromboplastin time (times the control value in seconds)	Zhou *et. al*[57].	Too many missing values, not included
Lactate dehydrogenase (U/L)	COVID-GRAM[41]; Xie *et.al*[37].	Too many missing values, not included
International normalized ratio	Zhou *et. al*[57].	Too many missing values, not included
Alanine aminotransferase (U/L)	EDRnet[58]; Chen *et. al*[89]; Sourij *et. al*[74]; Mei *et. al*[82].	Too many missing values, not included
Aspartate aminotransferase (U/L)		Too many missing values, not included
D-dimer	FAD-85[13]; NLAUD[16]; ANDC[52]; CSS score[54]; Hu *et. al*[55].	Different assays may compromise assessment, not included

Table S3. Variable selection based on generalized additive model

Variable	Deviance explained (%)	R-sq.(adj)	UBRE	D1-statistics (p-value)	D2-statistics (p-value)
All variables included	0.354	0.361	-0.324		
Sex at birth	0.354	0.361	-0.325	0.773	0.785
Age (years)	0.314	0.320	-0.284	0.000**	0.000**
Number of comorbities	0.353	0.361	-0.323	0.011**	0.011**
Respiratory rate (irpm)	0.351	0.358	-0.321	0.246	0.131
Heart rate (bpm)	0.350	0.357	-0.320	0.047**	0.122
Systolic blood pressure (mm Hg)	0.353	0.361	-0.324	0.217	0.244
Glasgow coma score	0.353	0.360	-0.324	0.995	1.000
SF ratio	0.333	0.339	-0.303	0.000**	0.000**
C-reactive protein (mg/L)	0.347	0.355	-0.318	0.006**	0.019**
Hemoglobin (g/L)	0.348	0.358	-0.321	0.069	0.087
NL ratio	0.351	0.359	-0.323	0.966	0.840
Platelet count (10^9/L)	0.335	0.344	-0.308	0.000**	0.000**
Creatinine (mg/dL)	0.354	0.361	-0.325	1.000	1.000
BUN (mg/dL)	0.347	0.355	-0.320	0.000**	0.001**
Lactate (mmol/L)	0.348	0.356	-0.320	0.144	0.459
Sodium (mmol/L)	0.352	0.359	-0.324	0.689	0.957
Bicarbonate (mEq/L)	0.353	0.360	-0.325	0.999	1.000
pH	0.352	0.360	-0.323	0.805	0.925
pO2 (mmHg)	0.349	0.358	-0.321	0.554	0.678
pCO2 (mmHg)	0.353	0.361	-0.324	0.996	1.000

BUN: blood urea nitrogen; UBRE: Unbiased risk estimator; D1: multivariate Wald test; D2: pools test statistics from the repeated analyses; NL: neutrophils-to-lymphocytes count ratio; SF: SpO_2/FiO_2 ratio

** Variable included in final model (p-value < 0.05)

Table S4. L1 penalized shrunk coefficients and scaled coefficients from LASSO logistic regression

Variable	Coefficients	Scaled coefficients (× 3)
Age (years)		
< 60	-	0
60 - 69	0.413	1
70 - 79	0.935	3
≥ 80	1.666	5
Number of comorbidities		
≤ 1	-	0
> 1	0.353	1
SF ratio		
> 315	-	0
>235 – 315	0.431	1
>150 – 235	1.001	3
≤ 150	1.880	6
C reactive protein (mg/L)		
< 100	-	0
≥ 100	0.476	1
Blood urea nitrogen (mg/dL)		
< 42	-	0
≥ 42	0.905	3
Platelet count (10^9/L)		
> 150	-	0
100 -150	0.288	1
< 100	0.667	2
Heart rate (bpm)		
≤ 90	-	0
91 – 130	0.185	1
≥ 131	0.503	2
Intercept	-2.965	-9

LASSO: least absolute shrinkage and selection operator logistic regression, SF ratio: SpO_2/FiO_2 ratio

Table S5. Sensitivity analysis - Discrimination and model overall performance within complete cases

Model	Derivation cohort		Brazilian validation cohort	
	AUROC (95%CI)	**Brier score**	**AUROC (95%CI)**	**Brier score**
GAM	0.871 (0.866; 0.875)	0.108	0.880 (0.878; 0.887)	0.094
LASSO	0.824 (0.792; 0.856)	0.115	0.858 (0.793; 0.922)	0.092
ABC_2-SPH	0.841 (0.824; 0.858)	0.114	0.852 (0.820; 0.884)	0.107

GAM: generalized additive models; LASSO: least absolute shrinkage and selection operator logistic regression

Table S6. TRIPOD checklist for transparent reporting on a multivariable prognostic model.

Section/topic	Item	Checklist item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	13
Introduction			
Background and objective	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models	15
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both	15-16
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable	16
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up	16-17
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres	17
	5b	Describe eligibility criteria for participants	16-17
	5c	Give details of treatments received, if relevant	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed	17
	6b	Report any actions to blind assessment of the outcome to be predicted	NA
Predictors	7a	Clearly define all predictors used in developing the multivariable prediction model, including how and when they were measured	17
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors	NA
Sample size	8	Explain how the study size was arrived at	NA

Section/topic	Item	Checklist item	Page
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method	18
Statistical analysis methods	10a	Describe how predictors were handled in the analyses	18-19
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation	18-19
	10c	For validation, describe how the predictions were calculated	19
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models	19-20
	10e	Describe any model updating (e.g., recalibration) arising from the validation, if done	NA
Risk groups	11	Provide details on how risk groups were created, if done	19-20
Development vs. validation	12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors	19-20
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful	21, Figure 1
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome	21, Table 1
	13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome)	Table 1
Model development	14a	Specify the number of participants and outcome events in each analysis	Table 1
	14b	If done, report the unadjusted association between each candidate predictor and outcome	NA
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point)	Table S4
	15b	Explain how to use the prediction model	Pages 28-29, Table 2
Model performance	16	Report performance measures (with CIs) for the prediction model	Table 4, Table S5
Model updating	17	If done, report the results from any model updating (i.e., model specification, model performance)	NA
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per	27-28

		predictor, missing data)	
Interpretation	19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	24-27
	19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence	24-28
Implications	20	Discuss the potential clinical use of the model and implications for future research	28-30
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets	24-30
Funding	22	Give the source of funding and the role of the funders for the present study	31

Table S7. Risk of bias assessment using PROBAST checklist

Domain and Item	Checklist item	Development	Brazilian validation
Participants			
1.1	Were appropriate data sources used, e.g., cohort, RCT, or nested case–control study data?	Yes (a cohort design has been used)	Yes (a cohort design has been used)
1.2	Were all inclusions and exclusions of participants appropriate?	Yes (participants correspond to unselected participants of interest)	Yes (participants correspond to unselected participants of interest)
Risk of bias introduced by participants or data sources: low risk of bias.			
Predictors			
2.1	Were predictors defined and assessed in a similar way for all participants?	Yes (definitions of predictors and their assessment were similar for all participants)	Yes (definitions of predictors and their assessment were similar for all participants)
2.2	Were predictor assessments made without knowledge of outcome data?	Yes (outcome information was stated as not used during predictor assessment)	Yes (outcome information was stated as not used during predictor assessment)
2.3	Are all predictors available at the time the model is intended to be used?	Yes (all included predictors were available at the time the model was intended to be used for prediction)	Yes (all included predictors were available at the time the model was intended to be used for prediction)
Risk of bias introduced by predictors or their assessment: low risk of bias.			
Outcome			
3.1	Was the outcome determined appropriately?	Yes (objective outcome was used: mortality)	Yes (objective outcome was used: mortality)
3.2	Was a prespecified or standard outcome definition used?	Yes (objective outcome was used: mortality)	Yes (objective outcome was used: mortality)
3.3	Were predictors excluded from the outcome definition?	Yes (none of the predictors are included in the outcome definition)	Yes (none of the predictors are included in the outcome definition)
3.4	Was the outcome defined and determined in a similar way for all participants?	Yes (outcomes were defined and determined in a similar way for all participants)	Yes (outcomes were defined and determined in a similar way for all participants)
3.5	Was the outcome determined without knowledge of predictor information?	Yes (predictor information was not known when determining the	Yes (predictor information was not known when determining the

		outcome status)	outcome status)
3.6	Was the time interval between predictor assessment and outcome determination appropriate?	Yes (time interval between predictor assessment and outcome determination was appropriate)	Yes (time interval between predictor assessment and outcome determination was appropriate)
Risk of bias introduced by predictors or their assessment: low risk of bias.			
Analysis			
4.1	Were there a reasonable number of participants with the outcome?	Yes (high number of events per variable).	Yes (number of participants with the outcome is ≥100)
4.2	Were continuous and categorical predictors handled appropriately?	Yes (continuous predictors are examined for nonlinearity using thin-plate splines and then categorical predictor groups were defined using widely accepted cut points, current evidence and/or categories defined in stablished rapid scoring systems).	Yes (predictors were used as in the development model).
4.3	Were all enrolled participants included in the analysis?	Yes (all participants enrolled in the study were included in the data analysis).	Yes (all participants enrolled in the study are included in the data analysis).
4.4	Were participants with missing data handled appropriately?	Yes (missing values were handled using multiple imputation methods)	Yes (missing values are handled using multiple imputation methods)
4.5	Was selection of predictors based on univariable analysis avoided?	Yes (the predictors were not selected on the basis of univariable analysis prior to multivariable modeling)	NA
4.6	Were complexities in the data (e.g., censoring, competing risks, sampling of control participants) accounted for appropriately?	Yes (a full cohort approach was used - median follow-up time was 7 days)	Yes (a full cohort approach was used - median follow-up time was 7 days)
4.7	Were relevant model performance measures evaluated appropriately?	Yes (both calibration and discrimination were evaluated appropriately)	Yes (both calibration and discrimination were evaluated appropriately)
4.8	Were model overfitting and optimism in model performance accounted for?	Yes (10-fold cross-validation have been used).	NA
4.9	Do predictors and their assigned weights in	Yes (the predictors and regression	NA

	the final model correspond to the results from the reported multivariable analysis?	coefficients in the final model correspond to reported results from multivariable analysis)

Risk of bias introduced by the analysis: low risk of bias.

Table S8. STROBE Statement

	Item No	Recommendation	Pg
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	01
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	13-14
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	15
Objectives	3	State specific objectives, including any prespecified hypotheses	15-16
Methods			
Study design	4	Present key elements of study design early in the paper	16-17
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	16-17
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	16-17
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	16-18
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	16-21
Bias	9	Describe any efforts to address potential sources of bias	16-17
Study size	10	Explain how the study size was arrived at	16-17
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	18-20
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	16-21
		(*b*) Describe any methods used to examine subgroups and interactions	21-23
		(*c*) Explain how missing data were addressed	18
		(*d*) If applicable, explain how loss to follow-up was addressed	16-20
		(*e*) Describe any sensitivity analyses	19-20
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	21-22 and table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	Table 1
Outcome data	15*	Report numbers of outcome events or summary measures over time	21-24
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 1
		(*b*) Report category boundaries when continuous variables were categorized	Table 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	24-27
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	27-28
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	24-30
Generalisability	21	Discuss the generalisability (external validity) of the study results	24-27
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	31

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Table S9. Reasons for exclusion of other scores in the comparison

Study	Included?
Halalau[68]	No. Congenital heart disease is not available.
Fumagalli[10]	No. Depression and dementia were not categorical variables in the present study.
~~Knight[36]~~	~~No. Dementia was collected as a free-text field, and could not be categorized up to the data this study was submitted.~~
Liang[41]	No. Composite outcome.
Nicholson[51]	No. Mean corpuscular volume is not available.
Garibaldi[73]	No. Nursing home resident and BMI are not available.
Sourij[74]	No. Arterial occlusive disease is not available as a categorical variable.
Gavelli[67]	No. SpO2 and respiratory rate after 15-minute trial with oxygen not available.
Kazemi[75]	No. Comorbidities were not well defined in the original study, percentage of involvement included in CT score is subjective and peripheral involvement is not well defined.
Núñez-Gil[76]	No. Variables not clearly defined in the original study (renal failure and elevated C-reactive protein).
Allenbach[14]	No. Composite outcome.
Kim[15]	No. CK-MB not available.
Altschul[65]	No. IL-6 is not available, intercept was not provided for calculation.
Hajifathalian[44]	Yes
Wang J[13]	No. D-dimer assay is not described by the authors.
Zhou[16]	No. D-dimer assay is not described by the authors.
Goméz[77]	No. The authors did not provide all information necessary to calculate the score.
Galloway[69]	No. Ethnicity not available.
Bello-Chavolla[78]	No. As the score was developed considering outpatients and inpatients, the comparison would not be appropriate.
Weng[52]	No. D-dimer assay not described by the authors.
Ko[52]	No. Not all predictors are availabe, such as RDW.
Xie[37]	Yes
Yoo[79]	No. Troponin assay not described by the authors.
Zhang[38]	No. Very limited study, most included variables had OR with 95% CI including 1.0.
Yadaw[80]	No. Ethnicity is not available.
Shang[54]	No. D-dimer assay not described by the authors.
Faisal[81]	No. Authors did not provide enough information about how to

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	calculate the score.
Mei[82]	No. Total protein is not available.
Zhang[8]	Yes
Lu[83]	No. Score development included patients with confirmed and suspected COVD-19, a comparison would not be appropriate.
Soto-Mota[84]	No. Not clear the moment the score is meant to be used.
Yan[85]	Yes
Williams[86]	No. Hyperlipidemia is not available as a categorical variable.
Gue[87]	Yes
Das[88]	No. Variables such as province are not applicable for other populations.
Levy[59]	No. Authors did not provide enough information about how to calculate the score.
Chen[89]	No. Authors did not provide enough information about how to calculate the score.
Sarkar[90]	No. Some variables are applicable only to the Chinese population, in the beggiing og the pandemic.
Hu[55]	No. D-dimer assay is not described by the authors.