Supplementary table 1 TRIPOD Checklist Prediction Model Development

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.	3
Introduction			
Background and objectives	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.	5
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
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.	5
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	5
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	5
	5b	Describe eligibility criteria for participants.	5
	5c	Give details of treatments received, if relevant.	N/A
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
	6b	Report any actions to blind assessment of the outcome to be predicted.	N/A
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	6
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	N/A
Sample size	8	Explain how the study size was arrived at.	5
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	6
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	6
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	7
Risk groups	11	Provide details on how risk groups were created, if done.	6
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.	8
	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.	8
Model development	14a	Specify the number of participants and outcome events in each analysis.	8
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	9
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).	11
	15b	Explain how to the use the prediction model.	11
Model performance	16	Report performance measures (with CIs) for the prediction model.	9-10
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	11
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	11
Funding	22	Give the source of funding and the role of the funders for the present study.	15

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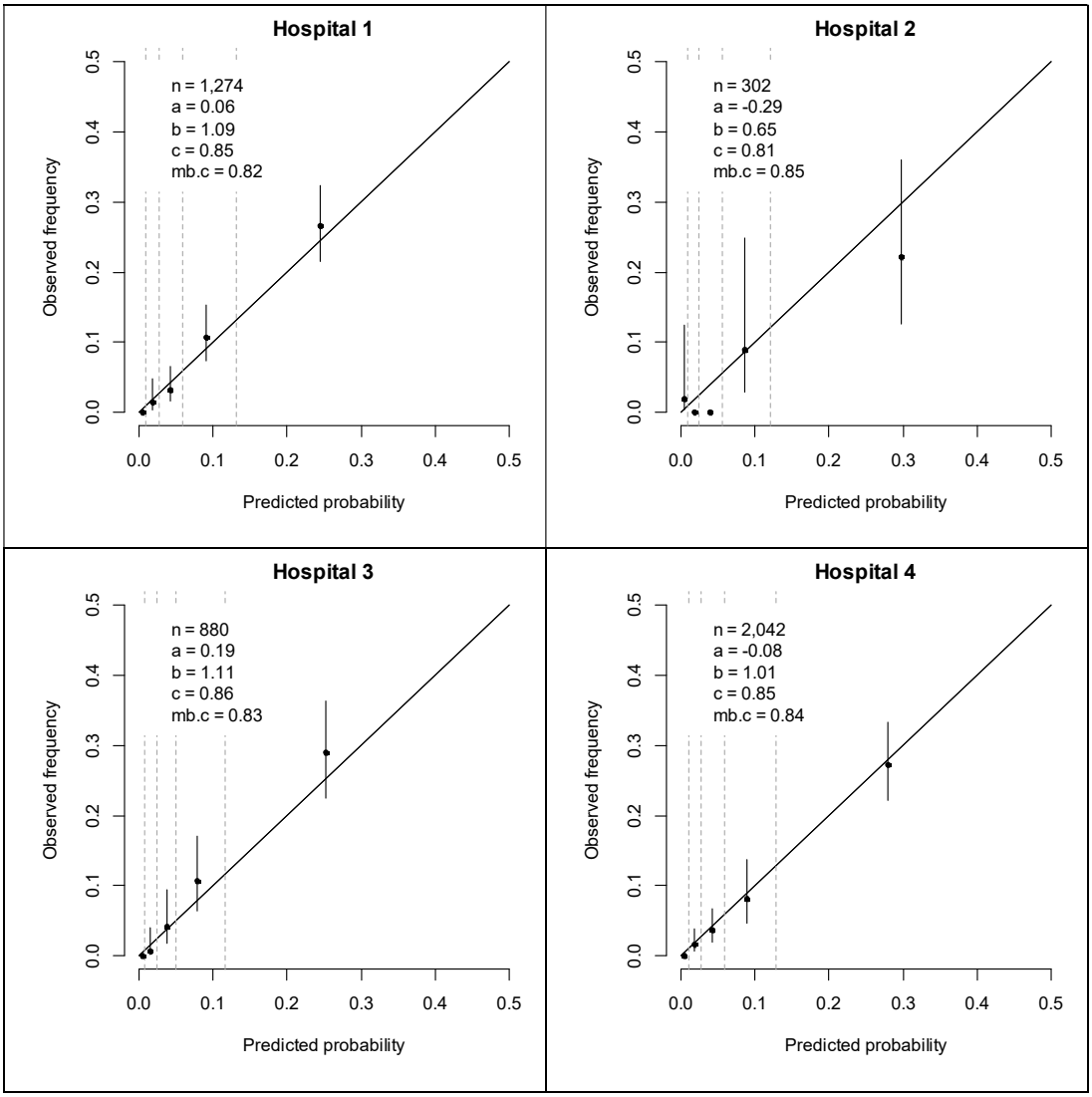
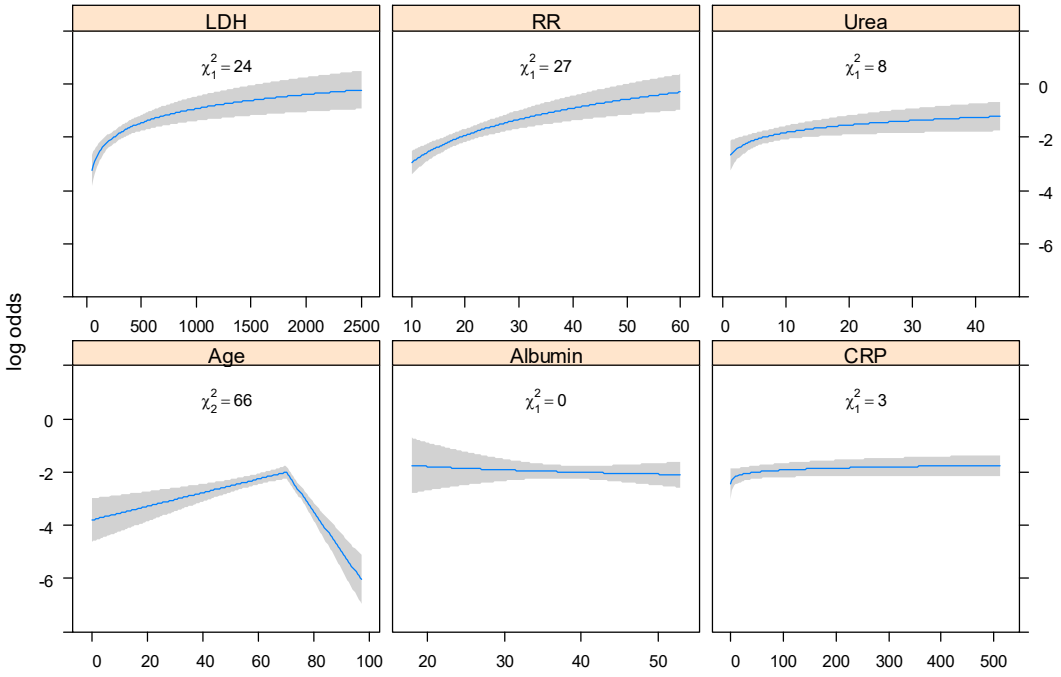
Supplementary figure 1 Apparent validation: Performance of COPE for predicting death in first wave patients Calibration plots of patients who were admitted from April up to and including August 2020 in 4 separate Dutch hospitals. n is number of patients; a = calibration intercept (0 is perfect); b = calibration slope (1 is perfect); c = AUC (0.5 is useless; 1 is perfect); mb.c = model-based AUC.



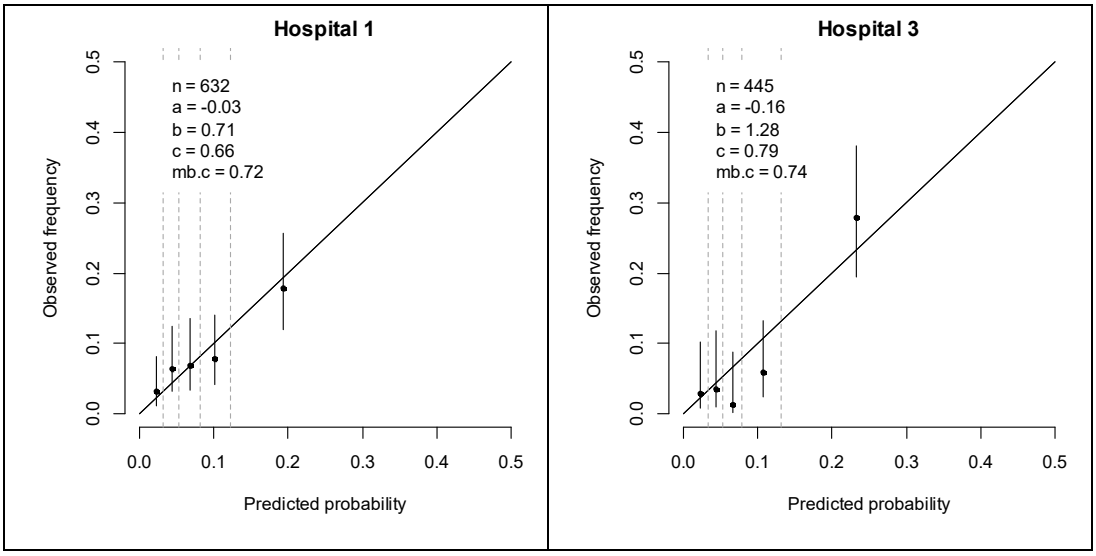
Supplementary figure 2 Multivariable effects of continuous predictors of ICU admission within 28 days

Predictions of the logarithm of the odds by continuous predictor levels, with other predictor levels set to the median. Age is modelled with a linear spline with a knot at age 70. Wald statistics are listed within each plot to express variable importance.



Supplementary figure 3 Apparent validation: Performance of COPE for predicting ICU in first wave

Calibration plots of patients who were admitted from April up to and including August 2020 in 2 separate Dutch hospitals. n is number of patients; a = calibration intercept (0 is perfect); b = calibration slope (1 is perfect); c = AUC (0.5 is useless; 1 is perfect); mb.c = model-based AUC.



Supplement 1 Description COPE web application

Background and aim: The COVID-19 pandemic is putting extraordinary pressure on emergency departments (EDs). Clinical prediction models have the potential to support decision making about hospital admission, but currently available models were recently assessed to contain a high risk of bias. We aimed to develop a simple and valid model for predicting mortality and need for ICU in patients who are suspected to have COVID-19 when presenting at the ED.

Methods: For model development, we included patients that presented at the ED and were admitted to 4 large Dutch hospitals with suspected COVID-19 between March and August 2020, the first wave of the pandemic in the Netherlands. Patients being transferred from or to other hospitals were excluded since information on predictors or outcomes was missing. The outcomes of interest were death and admission to ICU within 28 days. Based on prior literature we included patient characteristics (sex, age, BMI), vital parameters (oxygen saturation, systolic blood pressure, heart rate, respiratory rate [RR], body temperature) and blood test values (C-reactive protein [CRP], lactic dehydrogenase [LDH], D-Dimer, leucocytes, lymphocytes, monocytes, neutrophils, eosinophils, MCV, albumin, bicarbonate, creatinine, sodium, urea), all measured at ED admission, as potential predictors. Further we included month of admission to capture changes in outcomes over time. Logistic regression was used to obtain predicted probabilities of death and of being admitted to the ICU, both within 28 days after admission. Model performance was assessed with temporal validation in patients who presented between September and December 2020 (second wave). We assessed discriminative ability with the area under the operator receiver characteristic curve (AUC) and calibration with calibration plots, calibration intercepts, and calibration slopes. We used multiple imputation to account for missing predictor values.

Results: The development data included 5,831 patients who presented and were admitted at the ED up until August 2020, of whom 629 (10.8%) died and 5,070 (86.9%) were discharged within 28 days after admission. A simple model – named COVID Outcome Prediction in the Emergency Department (COPE) – with linear age and logarithmic transforms of RR, CRP, LDH, Albumin and Urea captured most of the ability to predict death within 28 days. Patients who were admitted in the first month of the pandemic in the Netherlands had substantially increased risk of death (odds ratio 2.06; 95% confidence interval 1.68-2.52). COPE was well-calibrated and showed good discrimination for predicting death in 3,252 patients in the second wave (AUC in 4 hospitals: 0.82; 0.82; 0.79; 0.83). Admission to ICU was fully recorded for 2,633 first wave patients in 2 hospitals (214 ICU admissions within 28 days). The same predictors captured most of the ability to predict ICU admission within 28 days. However, after the age of 70, the probability of being admitted to the ICU was decreasing with age, probably reflecting the decision not to admit older patients to the ICU. To predict the need for ICU admission – rather than

historically observed ICU admission – we kept a linear (decreasing) age effect after the age of 70 in the model, which will be ignored when making future predictions. COPE was well able to identify patients at high risk of needing IC in second wave patients below the age of 70 (AUC 0.84; 0.81), but overestimated ICU admission for low-risk patients. The models are implemented as a web-based application.

Conclusion: COPE, a simple tool based on 6 routinely measured predictors in the ED, is well able to predict mortality and ICU admission for patients who present to the ED with suspected COVID-19. COPE may help to inform patients and doctors when deciding on hospital admission.

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