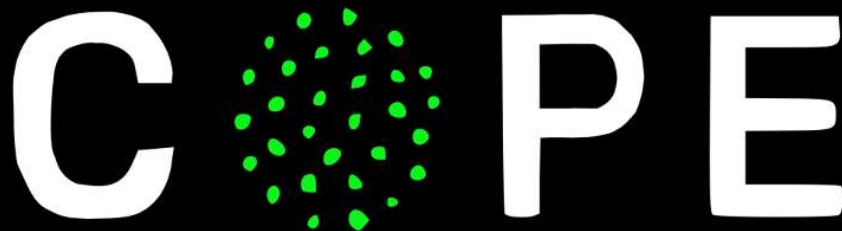


User manual

The logo for COPE, featuring the letters "C", "P", and "E" in a large, white, sans-serif font. The letter "O" is replaced by a cluster of green dots arranged in a circular pattern, resembling a virus or a molecular structure.

COVID Outcome Prediction in the Emergency department (COPE)

Version 2.1

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Information about the user manual

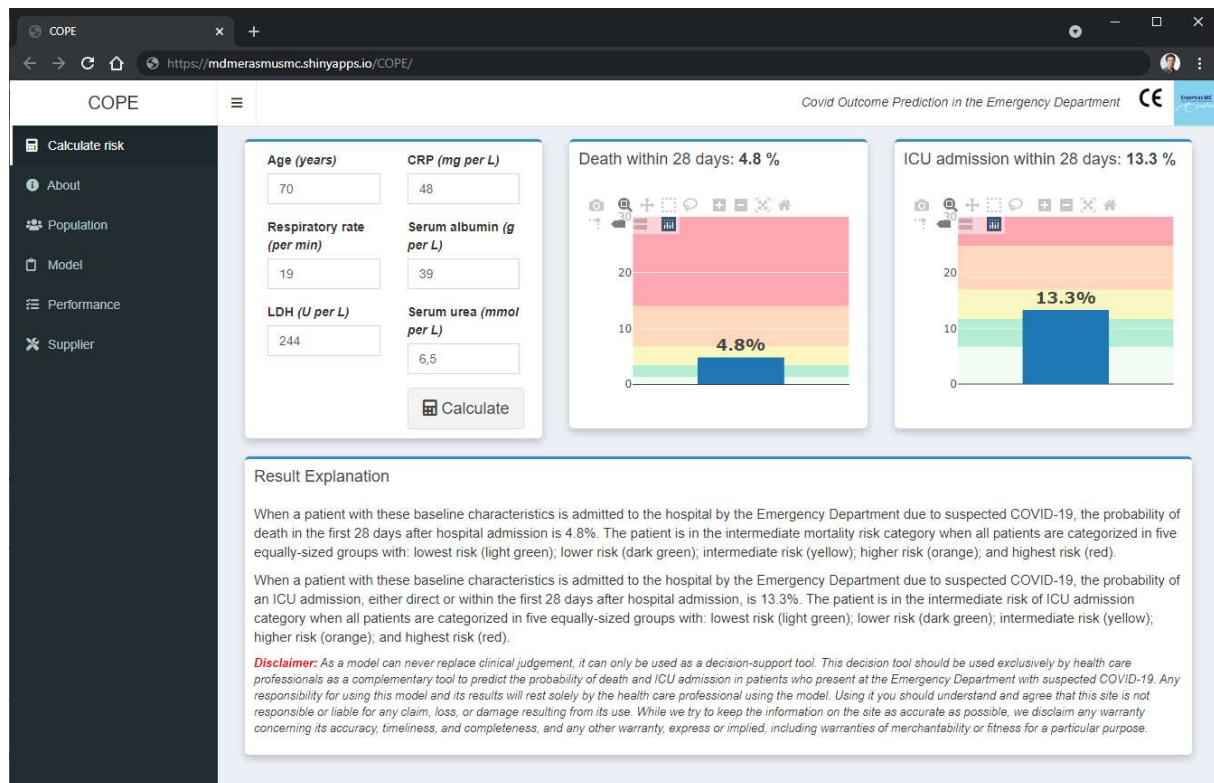
This user manual describes how to use "COVID Outcome Prediction in the Emergency Department (COPE)" and is intended for everyone who will work with the software.

Please read the operating instructions before using the COPE app.

If you have any questions, please contact Inner Join at erasmusmc@inner-join.nl.

1. Introduction

COPE (COVID Outcome Prediction in the Emergency department) is a simple tool based on 6 routinely measured predictors in the ED, that is well able to predict mortality and need for 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.



Cope should only be used by health care professionals.

Disclaimer: As a model can never replace clinical judgement, it can only be used as a decision-support tool. This decision tool should be used exclusively by health care professionals as a complementary tool to predict the probability of death and ICU admission in patients who present at the Emergency Department with suspected COVID-19. Any responsibility for using this model and its results will rest solely by the health care professional using the model. Using it you should understand and agree that this site is not responsible or liable for any claim, loss, or damage resulting from its use. While we try to keep the information on the site as accurate as possible, we disclaim any warranty concerning its accuracy, timeliness, and completeness, and any other warranty, express or implied, including warranties of merchantability or fitness for a particular purpose.

2. Intended application

2.1 Clinical benefit

COPE should provide accurate predictions of death and need for ICU admission within 28 days for patients who present to the emergency department with suspected COVID-19.

COPE may support emergency department physicians to identify high-risk patients – i.e. those at high risk of deterioration and/or death – requiring treatment in the ICU, intermediate-risk patients requiring admission to the clinical ward, and low-risk patients who can potentially be sent home.

2.2 The user

Emergency department physicians are end users of COPE.

2.3 The patient

All patients with suspected COVID-19 who present at the Emergency Department.

2.4 Contraindications

NA

3. Conformity

A Declaration of Conformity is in place for the COPE web app and the COPE native apps. Inner Join declares that the COPE apps meet the provision of the Regulation (EU) MDR 2017/745 for medical devices.

4. Description and operation


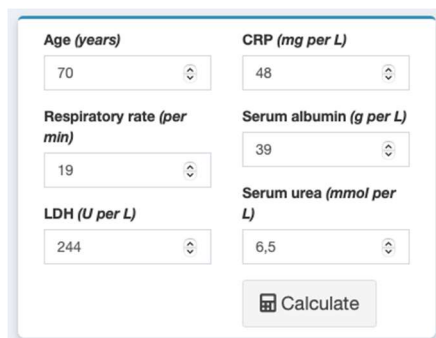
COPE (COVID Outcome Prediction in the Emergency department) is a simple tool based on 6 routinely measured predictors in the ED, that is well able to predict mortality and ICU admission for patients who present to the ED with suspected COVID-19. COPE may help to inform patients and doctors when deciding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

Here, we will distinguish the COPE webapp from the native COPE apps.

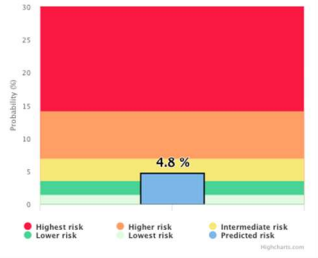
The native apps are developed in Ionic 5 and are compatible with iOS 11+ and Android 5+

The webapp is developed in R Shiny and is compatible with the latest 2 versions of Google Chrome, Mozilla Firefox, Safari and Internet Explorer.

This component of the app is used to input a patient's baseline characteristics required for the calculation of their mortality and ICU admission risk within 28 days of hospital admission:

Mobile Application	
Web Application	

COPE outputs the patient's mortality and ICU admission risk predictions based on the patient's input. The background colors are used to represent the patient's risk ranking compared to what was observed in the development population.

<p>Mobile Application</p>	<div data-bbox="566 347 1252 918"> <div> <p>Death within 28 days: 4.8%</p>  <p>ICU admission within 28 days: 13.3%</p>  <p>Result Explanation</p> <p>When a patient with these baseline characteristics is admitted to the hospital by the Emergency Department due to suspected COVID-19, the probability of death in the first 28 days after hospital admission is 4.8%. The patient is in the intermediate mortality risk category when all patients are categorized in five equally-sized groups with: lowest risk (light green); lower risk (dark green); intermediate risk (yellow); higher risk (orange); and highest risk (red).</p> <p>When a patient with these baseline characteristics is admitted to the hospital by the Emergency Department due to suspected COVID-19, the probability of an ICU admission, either direct or within the first 28 days after hospital admission, is 13.3%. The patient is in the intermediate risk of ICU admission category when all patients are categorized in five equally-sized groups with: lowest risk (light green); lower risk (dark green); intermediate risk (yellow); higher risk (orange); and highest risk (red).</p> <p>Disclaimer: As a model can never replace clinical judgement, it can only be used as a decision-support tool. This decision tool should be used exclusively by health care professionals as a complementary tool to predict the probability of death and ICU admission in patients who present at the Emergency Department with suspected COVID-19. Any responsibility for using this model and its results will rest solely by the health care professional using the model. Using it you should understand and agree that this site is not responsible or liable for any claim, loss, or damage resulting from its use. While we try to keep the information on the site as accurate as possible, we disclaim any warranty concerning its accuracy, timeliness, and completeness, and any other warranty, express or implied, including warranties of merchantability or fitness for a particular purpose.</p> </div> </div>
<p>Web Application</p>	<div data-bbox="566 974 1252 1590"> <div> <p>Death within 28 days: 4.8 %</p>  <p>ICU admission within 28 days: 13.3 %</p>  <p>Result Explanation</p> <p>When a patient with these baseline characteristics is admitted to the hospital by the Emergency Department due to suspected COVID-19, the probability of death in the first 28 days after hospital admission is 4.8%. The patient is in the intermediate mortality risk category when all patients are categorized in five equally-sized groups with: lowest risk (light green); lower risk (dark green); intermediate risk (yellow); higher risk (orange); and highest risk (red).</p> <p>When a patient with these baseline characteristics is admitted to the hospital by the Emergency Department due to suspected COVID-19, the probability of an ICU admission, either direct or within the first 28 days after hospital admission, is 13.3%. The patient is in the intermediate risk of ICU admission category when all patients are categorized in five equally-sized groups with: lowest risk (light green); lower risk (dark green); intermediate risk (yellow); higher risk (orange); and highest risk (red).</p> <p>Disclaimer: As a model can never replace clinical judgement, it can only be used as a decision-support tool. This decision tool should be used exclusively by health care professionals as a complementary tool to predict the probability of death and ICU admission in patients who present at the Emergency Department with suspected COVID-19. Any responsibility for using this model and its results will rest solely by the health care professional using the model. Using it you should understand and agree that this site is not responsible or liable for any claim, loss, or damage resulting from its use. While we try to keep the information on the site as accurate as possible, we disclaim any warranty concerning its accuracy, timeliness, and completeness, and any other warranty, express or implied, including warranties of merchantability or fitness for a particular purpose.</p> </div> </div>

5. Security

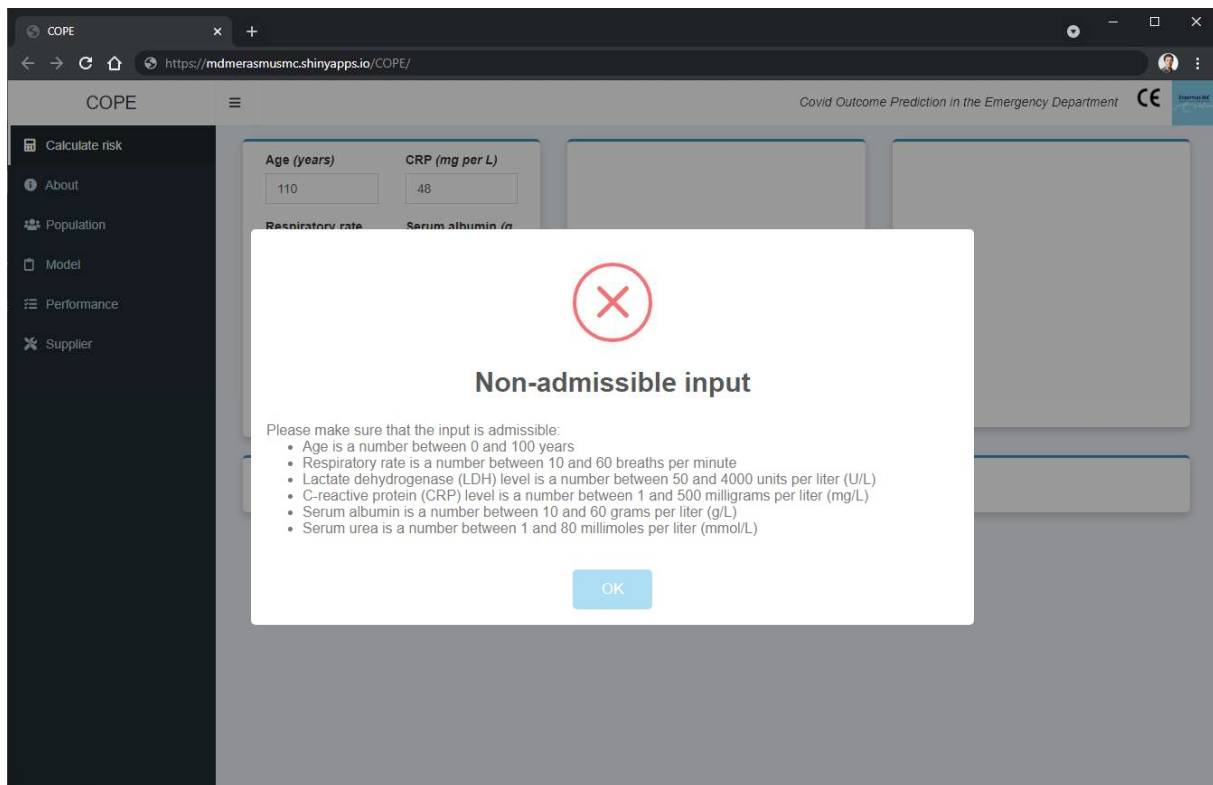
CAREFUL! Only specialist and trained staff are allowed to work with cope

Changes to the applications may only be implemented by Inner Join, or otherwise when written approval is gained.

5.1 Built-in safety measures

- COPE is CE certified. A Declaration of Conformity is in place for the COPE web app and the COPE native apps. Inner Join declares that the COPE apps meet the provision of the Regulation (EU) MDR 2017/745 for medical devices.
- Cope should only be used by health care professionals. Therefore, each COPE calculation is accompanied by a disclaimer: "As a model can never replace clinical judgement, it can only be used as a decision-support tool. This decision tool should be used exclusively by health care professionals as a complementary tool to predict the probability of death and ICU admission in patients who present at the Emergency Department with suspected COVID-19. Any responsibility for using this model and its results will rest solely by the health care professional using the model. Using it you should understand and agree that this site is not responsible or liable for any claim, loss, or damage resulting from its use. While we try to keep the information on the site as accurate as possible, we disclaim any warranty concerning its accuracy, timeliness, and completeness, and any other warranty, express or implied, including warranties of merchantability or fitness for a particular purpose."
- To prevent any coding errors in the COPE apps, a detailed test plan is in place for each new version of COPE. COPE 2.1 was successfully tested according to this test plan.

- COPE gives a warning and does not display any results when non-admissible input is entered:



5.2 Residual risks

The COPE apps meet the current safety requirements. However, even when used for the intended purposes and following all instructions, residual risks cannot be fully excluded.

- The web application may temporarily be unavailable when the server is down.

6. Storage

The source code of the webapp is saved on GitHub (USA).

The source code of the mobile apps is saved on GitLab (USA).

Inserted data is not being stored. When closing or refreshing the web browser all inserted data is deleted.

7. Installation

The webapp does not require installation and can be run in the latest 2 web browser versions of Google Chrome, Mozilla Firefox, Safari and Internet Explorer.


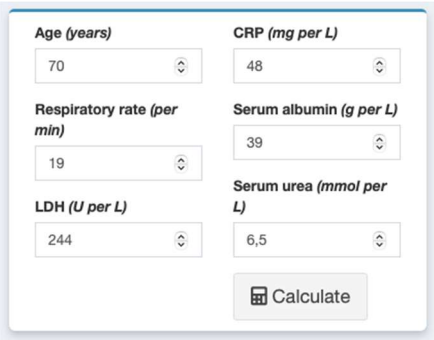
The mobile apps are installed through either the Google Play Store or the Apple Store.

8. Operation / instructions for use

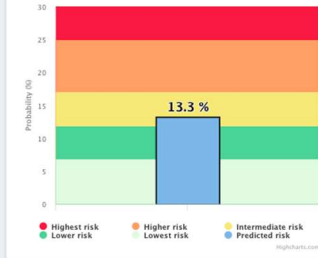
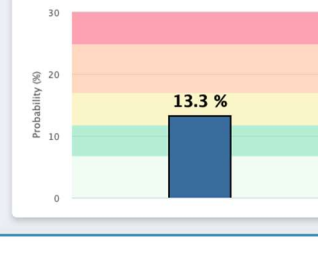
COPE starts in the “Calculate risk” tab. When a patient with suspected COVID-19 presents at the emergency department, enter the patient’s baseline characteristics. The necessary baseline characteristics together with their minimum and maximum values are:

Predictor	Minimum	Maximum
Age = Age (years)	0	100
RR = Respiratory rate (/min)	10	60
LDH = Lactatedehydrogenase (U/L)	50	4000
CRP = C-Reactive protein (mg/L)	1	500
Albumin = Serum Albumin (g/L)	10	60
Urea = Serum Urea (mmol/L)	1	80

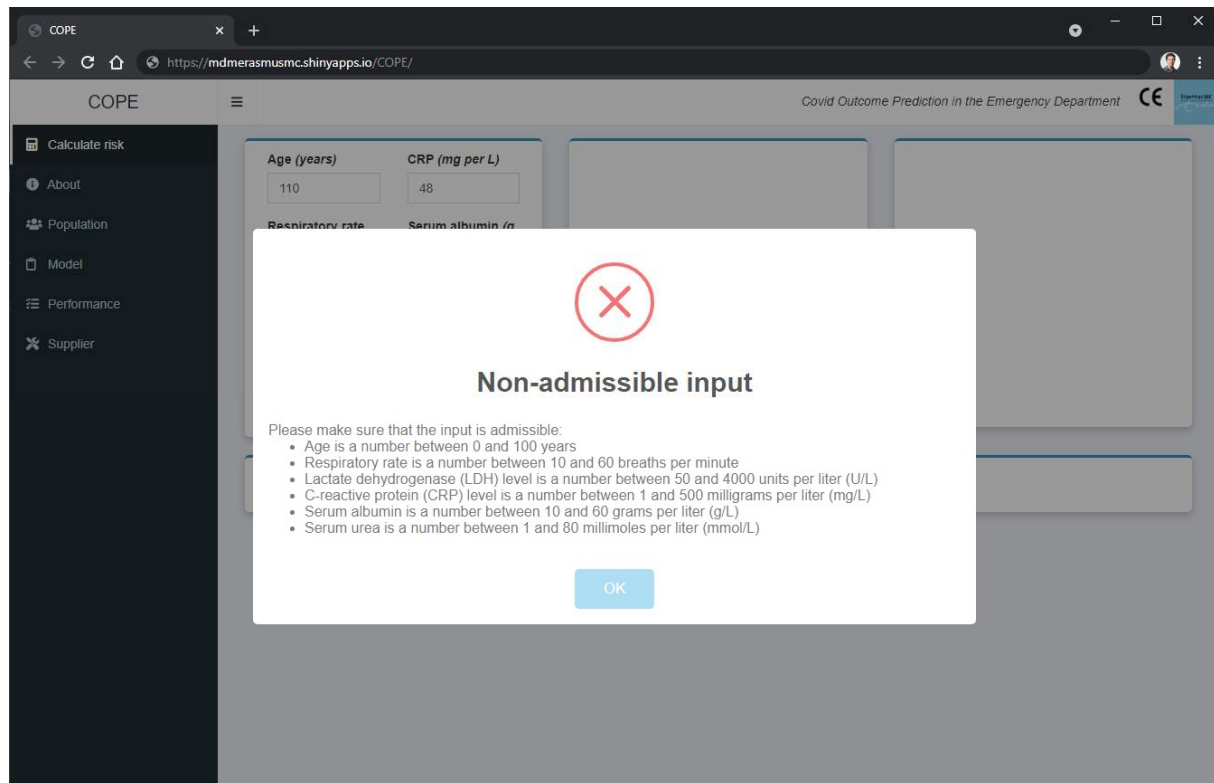
After filling out the 6 values, press the button “Calculate”:

<p>Mobile Application</p>	 <p>The mobile application interface shows a 'Risk Calculator' form. It contains six input fields with the following values: Age (years) 70, Respiratory rate (per min) 19, LDH (U per L) 244, CRP (mg per L) 48, Serum albumin (g per L) 39, and Serum urea (mmol per L) 6,5. A blue 'CALCULATE' button is at the bottom.</p>
<p>Web Application</p>	 <p>The web application interface shows a 'Risk Calculator' form. It contains six input fields with the following values: Age (years) 70, Respiratory rate (per min) 19, LDH (U per L) 244, CRP (mg per L) 48, Serum albumin (g per L) 39, and Serum urea (mmol per L) 6,5. A 'Calculate' button is at the bottom.</p>

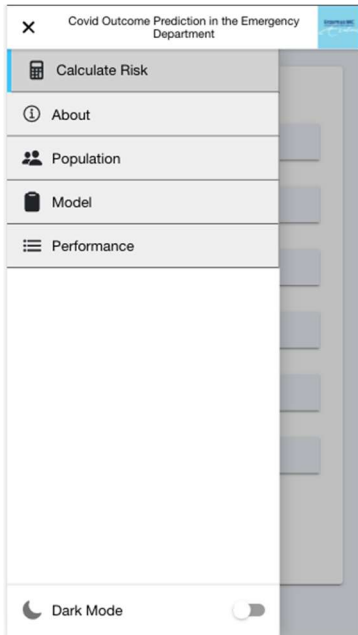
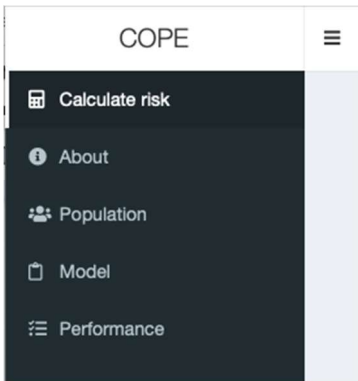
COPE returns the patient's mortality and ICU admission risk predictions based on the patient's input. The background colors are used to represent the patient's risk ranking compared to what was observed in the development population.

<p>Mobile Application</p>	<div data-bbox="566 347 1252 918"> <div> <p>Death within 28 days: 4.8%</p>  <p>ICU admission within 28 days: 13.3%</p>  <p>Result Explanation</p> <p>When a patient with these baseline characteristics is admitted to the hospital by the Emergency Department due to suspected COVID-19, the probability of death in the first 28 days after hospital admission is 4.8%. The patient is in the intermediate mortality risk category when all patients are categorized in five equally-sized groups with: lowest risk (light green); lower risk (dark green); intermediate risk (yellow); higher risk (orange); and highest risk (red).</p> <p>When a patient with these baseline characteristics is admitted to the hospital by the Emergency Department due to suspected COVID-19, the probability of an ICU admission, either direct or within the first 28 days after hospital admission, is 13.3%. The patient is in the intermediate risk of ICU admission category when all patients are categorized in five equally-sized groups with: lowest risk (light green); lower risk (dark green); intermediate risk (yellow); higher risk (orange); and highest risk (red).</p> <p>Disclaimer: As a model can never replace clinical judgement, it can only be used as a decision-support tool. This decision tool should be used exclusively by health care professionals as a complementary tool to predict the probability of death and ICU admission in patients who present at the Emergency Department with suspected COVID-19. Any responsibility for using this model and its results will rest solely by the health care professional using the model. Using it you should understand and agree that this site is not responsible or liable for any claim, loss, or damage resulting from its use. While we try to keep the information on the site as accurate as possible, we disclaim any warranty concerning its accuracy, timeliness, and completeness, and any other warranty, express or implied, including warranties of merchantability or fitness for a particular purpose.</p> </div> </div>
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COPE gives a warning and does not display any results when non-admissible input is entered:



For transparency, COPE also provides information. This information can be viewed using the menu:

<p>Mobile Application</p>	
<p>Web Application</p>	

Under the “About” tab, COPE provides background information about the COPE app:

<h2>Mobile Application</h2>	<h3>Abstract</h3> <p>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.</p> <p>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.</p> <p>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 ICU 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.</p>
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Under the “Population” tab, COPE provides aggregated information on the patients that were used to develop the COPE prediction models:

Name	Population Table																																																																																																																																																																																																																																				
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View Mobile Application	<div><div><div><div><div><div></div><div>Search</div></div></div><div><div><div>Baseline characteristics of development and validation patient cohorts. Status, "All patients (Overall)", "Discharged", "In hospital" and "Dead" are measured at 28 days after hospital admission.</div><div>Status at 28 days:All Statuses ▾</div><div>Items per page:22 ▾</div></div><div><table><tr><th>#</th><th>Status at 28 days</th><th>Variable</th><th>N</th><th>Missing</th><th>%</th><th>Me</th></tr><tr><td>1</td><td>Overall</td><td>Age (years)</td><td>5831</td><td>0</td><td>0</td><td>65.8</td></tr><tr><td>2</td><td>Overall</td><td>Albumin (g/L)</td><td>4936</td><td>895</td><td>15.35</td><td>38.6</td></tr><tr><td>3</td><td>Overall</td><td>Bicarbonate (mmol/L)</td><td>3182</td><td>2649</td><td>45.43</td><td>23.7</td></tr><tr><td>4</td><td>Overall</td><td>BMI (kg/ms)</td><td>2471</td><td>3360</td><td>57.62</td><td>27.0</td></tr><tr><td>5</td><td>Overall</td><td>Creatinine (μmol/L)</td><td>5375</td><td>456</td><td>7.82</td><td>103</td></tr><tr><td>6</td><td>Overall</td><td>CRP (mg/L)</td><td>5420</td><td>411</td><td>7.05</td><td>80.3</td></tr><tr><td>7</td><td>Overall</td><td>D.dimer (μg/L)</td><td>2072</td><td>3759</td><td>64.47</td><td>286</td></tr><tr><td>8</td><td>Overall</td><td>Eosinophils (x10^9/L)</td><td>4318</td><td>1513</td><td>25.95</td><td>0.08</td></tr><tr><td>9</td><td>Overall</td><td>HR (bpm)</td><td>3540</td><td>2291</td><td>39.29</td><td>92.3</td></tr><tr><td>10</td><td>Overall</td><td>LDH (U/L)</td><td>4764</td><td>1067</td><td>18.3</td><td>297</td></tr></table></div></div></div></div></div>	#	Status at 28 days	Variable	N	Missing	%	Me	1	Overall	Age (years)	5831	0	0	65.8	2	Overall	Albumin (g/L)	4936	895	15.35	38.6	3	Overall	Bicarbonate (mmol/L)	3182	2649	45.43	23.7	4	Overall	BMI (kg/ms)	2471	3360	57.62	27.0	5	Overall	Creatinine (μmol/L)	5375	456	7.82	103	6	Overall	CRP (mg/L)	5420	411	7.05	80.3	7	Overall	D.dimer (μg/L)	2072	3759	64.47	286	8	Overall	Eosinophils (x10^9/L)	4318	1513	25.95	0.08	9	Overall	HR (bpm)	3540	2291	39.29	92.3	10	Overall	LDH (U/L)	4764	1067	18.3	297																																																																																																																																																							
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View Web Application	<div><div><div><div><div>Search:</div><div></div></div><div>Table: Baseline characteristics of development patient cohort. Status, "Overall", "Discharged","In hospital" and "Dead" is measured at 28 days after hospital admission</div><div><table><tr><th>Status at 28 days</th><th>Variable</th><th>N</th><th>Missing</th><th>%</th><th>Mean</th><th>SD</th><th>Min</th><th>1st quartile</th><th>Median</th><th>3rd quartile</th><th>Max</th></tr><tr><td>1 Overall</td><td>Age (years)</td><td>5831</td><td>0</td><td>0.00</td><td>65.86</td><td>19.46</td><td>0.00</td><td>58.00</td><td>70.00</td><td>80.00</td><td>100.00</td></tr><tr><td>2 Overall</td><td>Albumin (g/L)</td><td>4936</td><td>895</td><td>15.35</td><td>38.63</td><td>5.38</td><td>12.50</td><td>35.50</td><td>39.00</td><td>42.00</td><td>58.00</td></tr><tr><td>3 Overall</td><td>Bicarbonate (mmol/L)</td><td>3182</td><td>2649</td><td>45.43</td><td>23.71</td><td>4.06</td><td>4.50</td><td>21.40</td><td>23.60</td><td>25.90</td><td>46.80</td></tr><tr><td>4 Overall</td><td>BMI (kg/m²)</td><td>2471</td><td>3360</td><td>57.62</td><td>27.01</td><td>5.76</td><td>11.24</td><td>23.32</td><td>26.20</td><td>29.80</td><td>61.30</td></tr><tr><td>5 Overall</td><td>Creatinine (μmol/L)</td><td>5375</td><td>456</td><td>7.82</td><td>103.99</td><td>82.72</td><td>14.00</td><td>66.00</td><td>84.00</td><td>111.00</td><td>1,710.00</td></tr><tr><td>6 Overall</td><td>CRP (mg/L)</td><td>5420</td><td>411</td><td>7.05</td><td>80.32</td><td>90.88</td><td>0.30</td><td>10.00</td><td>48.00</td><td>118.00</td><td>630.00</td></tr><tr><td>7 Overall</td><td>D.dimer (μg/L)</td><td>2072</td><td>3759</td><td>64.47</td><td>2,867.43</td><td>5,417.26</td><td>150.00</td><td>527.00</td><td>1,100.00</td><td>2,544.50</td><td>35,000.00</td></tr><tr><td>8 Overall</td><td>Eosinophils (x10^9/L)</td><td>4318</td><td>1513</td><td>25.95</td><td>0.08</td><td>0.20</td><td>0.00</td><td>0.00</td><td>0.03</td><td>0.10</td><td>5.60</td></tr><tr><td>9 Overall</td><td>HR (bpm)</td><td>3540</td><td>2291</td><td>39.29</td><td>92.32</td><td>21.12</td><td>2.00</td><td>78.00</td><td>90.00</td><td>103.00</td><td>210.00</td></tr><tr><td>10 Overall</td><td>LDH (U/L)</td><td>4764</td><td>1067</td><td>18.30</td><td>297.85</td><td>229.61</td><td>50.00</td><td>200.00</td><td>244.00</td><td>322.25</td><td>4,600.00</td></tr><tr><td>11 Overall</td><td>Leucocytes (x10^9/L)</td><td>5408</td><td>423</td><td>7.25</td><td>10.62</td><td>9.95</td><td>0.10</td><td>6.70</td><td>9.10</td><td>12.70</td><td>334.00</td></tr><tr><td>12 Overall</td><td>Lymphocytes (x10^9/L)</td><td>4893</td><td>938</td><td>16.09</td><td>1.58</td><td>5.65</td><td>0.00</td><td>0.66</td><td>1.04</td><td>1.60</td><td>192.60</td></tr><tr><td>13 Overall</td><td>Male sex</td><td>5831</td><td>0</td><td>0.00</td><td>0.57</td><td>0.50</td><td>0.00</td><td>0.00</td><td>1.00</td><td>1.00</td><td>1.00</td></tr><tr><td>14 Overall</td><td>MCV (fL)</td><td>5406</td><td>425</td><td>7.29</td><td>90.62</td><td>6.86</td><td>56.00</td><td>87.00</td><td>90.00</td><td>94.00</td><td>131.00</td></tr><tr><td>15 Overall</td><td>Monocytes (x10^9/L)</td><td>4100</td><td>1731</td><td>29.69</td><td>0.75</td><td>0.56</td><td>0.00</td><td>0.44</td><td>0.67</td><td>0.95</td><td>12.93</td></tr><tr><td>16 Overall</td><td>Neutrophils (x10^9/L)</td><td>4873</td><td>958</td><td>16.43</td><td>6.33</td><td>5.32</td><td>0.00</td><td>2.19</td><td>5.60</td><td>8.96</td><td>85.89</td></tr><tr><td>17 Overall</td><td>RR (/min)</td><td>3403</td><td>2428</td><td>41.64</td><td>20.42</td><td>6.80</td><td>1.00</td><td>16.00</td><td>19.00</td><td>23.33</td><td>101.00</td></tr><tr><td>18 Overall</td><td>Saturation (%)</td><td>3462</td><td>2369</td><td>40.63</td><td>95.41</td><td>3.66</td><td>16.00</td><td>94.00</td><td>95.80</td><td>97.50</td><td>100.00</td></tr></table></div></div></div></div>	Status at 28 days	Variable	N	Missing	%	Mean	SD	Min	1st quartile	Median	3rd quartile	Max	1 Overall	Age (years)	5831	0	0.00	65.86	19.46	0.00	58.00	70.00	80.00	100.00	2 Overall	Albumin (g/L)	4936	895	15.35	38.63	5.38	12.50	35.50	39.00	42.00	58.00	3 Overall	Bicarbonate (mmol/L)	3182	2649	45.43	23.71	4.06	4.50	21.40	23.60	25.90	46.80	4 Overall	BMI (kg/m²)	2471	3360	57.62	27.01	5.76	11.24	23.32	26.20	29.80	61.30	5 Overall	Creatinine (μmol/L)	5375	456	7.82	103.99	82.72	14.00	66.00	84.00	111.00	1,710.00	6 Overall	CRP (mg/L)	5420	411	7.05	80.32	90.88	0.30	10.00	48.00	118.00	630.00	7 Overall	D.dimer (μg/L)	2072	3759	64.47	2,867.43	5,417.26	150.00	527.00	1,100.00	2,544.50	35,000.00	8 Overall	Eosinophils (x10^9/L)	4318	1513	25.95	0.08	0.20	0.00	0.00	0.03	0.10	5.60	9 Overall	HR (bpm)	3540	2291	39.29	92.32	21.12	2.00	78.00	90.00	103.00	210.00	10 Overall	LDH (U/L)	4764	1067	18.30	297.85	229.61	50.00	200.00	244.00	322.25	4,600.00	11 Overall	Leucocytes (x10^9/L)	5408	423	7.25	10.62	9.95	0.10	6.70	9.10	12.70	334.00	12 Overall	Lymphocytes 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Under the “Description” tab, COPE provides the exact mathematical formulas used for the prediction of risks:

<p>Mobile Application</p>	<div data-bbox="778 309 1173 1052"> <p>log = natural logarithm; exp = natural exponential</p> <p>Mortality</p> <p>The probability of mortality within 28 days is predicted using a logistic regression model. The linear predictor of the model is given by:</p> $\begin{aligned} LP_{mort} = & -13.6 \\ & + 0.04575 \times Age \\ & + 1.654 \times \log(RR) \\ & + 1.197 \times \log(LDH) \\ & + 0.1688 \times \log(CRP) \\ & - 1.585 \times \log(Albumin) \\ & + 0.5953 \times \log(Urea) \end{aligned}$ <p>The probability of death within 28 days is:</p> $Pr(Death) = \frac{1}{1 + \exp(-LP_{mort})}$ <p>ICU admission</p> <p>The probability of admission to the ICU within 28 days is predicted using a re-calibrated version of the model for 28-day mortality. More specifically, the linear predictor of the model for ICU admission is given from:</p> $LP_{ICU} = -0.08949 + 0.5790 \times LP_{mort}$ <p>The probability of necessary ICU admission within 28 days is:</p> $Pr(ICU) = \frac{1}{1 + \exp(-LP_{ICU})}$ </div>
<p>Web Application</p>	<div data-bbox="582 1115 1372 1512"> <p>Mortality</p> <p>The probability of mortality within 28 days was estimated using a logistic regression model. The linear predictor of the model is given by:</p> $\begin{aligned} LP_{mort} = & -13.6 \\ & + 0.046 \times Age + 1.654 \times \log(RR) \\ & + 0.169 \times \log(CRP) + 1.197 \times \log(LDH) \\ & - 1.585 \times \log(Albumin) + 0.595 \times \log(Urea) \end{aligned}$ <p>Then the probability of death in 28 days is given from:</p> $Pr(Death) = \frac{1}{1 + \exp(-LP_{mort})}$ <p>ICU admission</p> <p>The probability of admission to the ICU within 28 days was estimated using a re-calibrated version of the model for 28-day mortality. More specifically, the linear predictor of the model for ICU admission is given from:</p> $LP_{ICU} = -0.089 + 0.597 \times LP_{mort}$ <p>Then, the probability for 28-day ICU admission can be estimated from:</p> $Pr(ICU) = \frac{1}{1 + \exp(-LP_{ICU})}$ <p><small>Note: here log is the natural logarithm and exp is the natural exponential</small></p> </div>

Under the “Performance” tab, COPE provides commonly used performance evaluation metrics of the underlying risk prediction models:

<p>Mobile Application</p>	<div> <div> <div> <div>Calibration plot for Mortality</div> </div> <div> <div>Calibration plot for ICU admission</div> </div> </div> <div> <div>Evaluation metrics</div> <p>The evaluation metrics are all based on temporal validation in second wave patients, that is, COPE was fitted in first wave patients admitted until August 2020 and validated in second wave patients admitted since September 2020 Calibration plots visualize the agreement between predicted and observed 28-day mortality / ICU admission in five equally-sized groups of predicted risk. The calibration intercept (a; ideally a=0) indicates the level of average underestimation (a<0) or overestimation (a>0) of the model. The calibration slope (b; ideally b=1) indicates a weaker than expected strength of the association between the predictors and the outcome (b<1; “overfitting”) or a stronger than expected strength of the association between the predictors and the outcome (b>1; “underfitting”) of the model. The c-index (c; between 0.5 and 1) indicates the discriminative ability of the model, that is the ability to separate low-risk from high-risk patients.</p> </div> </div>
<p>Web Application</p>	<div> <div> <div> <div>Calibration plot for mortality</div> </div> <div> <div>Calibration plot for ICU admission</div> </div> </div> <div> <div>Evaluation metrics</div> <p>The evaluation metrics are all based on temporal validation in second wave patients, that is, COPE was fitted in first wave patients admitted until August 2020 and validated in second wave patients admitted since September 2020 Calibration plots visualize the agreement between predicted and observed 28-day mortality / ICU admission in five equally-sized groups of predicted risk. The calibration intercept (a; ideally a=0) indicates the level of average underestimation (a<0) or overestimation (a>0) of the model. The calibration slope (b; ideally b=1) indicates a weaker than expected strength of the association between the predictors and the outcome (b<1; “overfitting”) or a stronger than expected strength of the association between the predictors and the outcome (b>1; “underfitting”) of the model. The c-index (c; between 0.5 and 1) indicates the discriminative ability of the model, that is the ability to separate low-risk from high-risk patients.</p> </div> </div>

9. Failures

Failure	Possible cause	Solution
Native app won't work in future OS versions	Incompatibility code with OS	Contact supplier and department about possible solutions (SLA)
Web app won't work in future web browser versions	Incompatibility code with new browser versions	Contact supplier and department about possible solutions (SLA)

If the fault has not been resolved using the table or if in doubt, please contact Inner Join at erasmusmc@inner-join.nl.

10. Maintenance

The current version is COPE 2.1. The version is visible under “About” tab.

11. Disposal / de-installation

The mobile app can be deinstalled using standard mobile phone functionality.