



Early View

Original research article

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Validation of the qSOFA and CRB-65 in SARS-CoV-2 infected community-acquired pneumonia

Tina Richter¹, Falko Tesch², Jochen Schmitt², Dirk Koschel¹, and Martin Kolditz¹

¹ Division of Pulmonology, Medical Department I, University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany

² Dresden University Centre for Evidence-Based Healthcare, University Hospital and Faculty of Medicine Carl Gustav Carus, Technische Universität Dresden, Germany

Corresponding author: Martin Kolditz, Division of Pulmonology, Medical Department I, University Hospital Carl Gustav Carus, Fetscherstr. 74, 01307 Dresden, Germany, Telephone: +49-351-4583417, FAX: +49-351-4585892, Email: martin.kolditz@uniklinikum-dresden.de

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Take home message:

Mortality and mechanical ventilation rates are higher in SARS-CoV-2 positive compared to SARS-CoV-2 negative CAP. Only scores with age criterion (CRB-65 and qSOFA-65) provide adequate mortality prediction, but sensitivity is low for mechanical ventilation.

This article has an online data supplement.

Key words: community-acquired pneumonia, COVID-19, SARS-CoV-2, risk stratification, mortality, mechanical ventilation

Abstract

Rationale

Prognostic accuracy of the qSOFA and CRB-65 risk scores has not been widely evaluated in SARS-CoV-2 infected compared to SARS-CoV-2 non-infected community-acquired pneumonia (CAP).

Objectives

The aim was to validate the qSOFA(-65) and CRB-65 scores in a large cohort of SARS-CoV-2 infected and non-infected CAP patients.

Methods

We included all cases with CAP hospitalized in 2020 from the German nationwide mandatory quality assurance program and compared SARS-CoV-2 infected with non-infected cases. We excluded cases with unclear SARS-CoV-2 infection state, transferred to another hospital or on mechanical ventilation (MV) during admission. Predefined outcomes were hospital mortality and need of MV.

Results

Among 68,594 SARS-CoV-2 infected patients, hospital mortality (22.7%) and MV (14.9%) was significantly higher when compared to 167,880 SARS-CoV-2 negative patients (15.7% and 9.2%, respectively). All CRB-65 and qSOFA criteria were associated with both outcomes, and age dominated mortality prediction in SARS-CoV-2 (relative risk >9). Scores including the age-criterion had higher AUCs for mortality in SARS-CoV-2 positive (e.g. CRB-65 AUC 0.76) compared to SARS-CoV-2 negative (AUC 0.68) patients, and NPV was highest for qSOFA-65 = 0 (98.2%). Sensitivity for MV prediction was poor with all scores (AUCs 0.59-0.62), and NPVs were insufficient (qSOFA-65=0 missed 1490/10,198~ 15% patients with MV). Results were similar when excluding frail and palliative patients.

Conclusions

Hospital mortality and MV rates were higher in SARS-CoV-2 positive compared to SARS-CoV-2 negative CAP. For SARS-CoV-2 positive CAP, the CRB-65 and qSOFA-65 scores showed adequate prediction of mortality, but not of MV.

Introduction

Since 2019 the COVID-19 pandemic causes an extraordinary strain on global health systems. Despite changing epidemiology, SARS-CoV-2 remains one potential pathogen amongst others causing community-acquired pneumonia (CAP). As with bacterial CAP, SARS-CoV-2 pneumonia severity is highly variable with potential disease courses from mild to critical disease. Thus, adequate risk scoring is essential for initial assessment.

Although risk stratification in SARS-CoV-2 positive CAP has been studied recently, its implementation still remains poorly defined, and most guidelines do not recommend specific risk scores for COVID-19 [1-3]. A systematic review updated in July 2022 found 265 prognostic models for mortality and 84 for progression to severe or critical course. However, many of these studies were at high or unclear risk of bias [4]. The best predictive performance had been shown with specific, but often complicated risk scores like the 4C scores involving 8 to 11 variables [4-6]. As CAP aetiology often is not established at first presentation, most patients presenting with CAP in busy emergency departments will initially be evaluated according to CAP algorithms. The current German CAP guideline [7] recommends initial risk screening including the CRB-65 score and evaluation of potential sepsis with the qSOFA. Both scores only partially have been validated for initial assessment of SARS-CoV-2 CAP with conflicting results in recent studies [5, 8-12]. Additionally, prediction models show heterogeneous results according to the specified outcome (mortality vs. severe disease / mechanical ventilation).

The aim of the present study was to evaluate the accuracy of the risk scores qSOFA, qSOFA-65 and CRB-65 for prediction of hospital mortality or mechanical ventilation in a large, representative population of hospitalized SARS-CoV-2 positive and negative CAP patients.

Methods

Database

We used the database of the German nationwide mandatory quality assurance program according to §136 SGB V. Here, all hospitals in Germany are required to document clinical routine data from all hospitalized CAP cases in a pre-specified electronic data sheet, as described previously [13]. CAP cases are identified by ICD codes as listed elsewhere [13];

patients with nosocomial pneumonia and with immunosuppression are excluded. Cases admitted to emergency department but not hospitalized are not recorded. The study was approved by the ethic committee of the TU Dresden (EK 609122017).

Study population

As a reference, we included all hospitalised patients with CAP with or without SARS-CoV-2 infection from the study period of January 1st 2020 to December 31st 2020. SARS-CoV-2 infection was defined as documented code U07.1 (SARS-CoV-2 confirmed by laboratory test) together with the qualifying pneumonia code. Patients with unclear SARS-CoV-2 status, defined as SARS-CoV-2 infection with missing laboratory confirmation (U07.2) or post-COVID conditions (U07.3-5) were excluded from all analyses.

For our main cohorts, we further excluded all patients who had been transferred to another hospital (no outcome parameter) or were on invasive ventilation on admission (no meaningful risk scoring). Applying those eligibility criteria, two main CAP cohorts from SARS-CoV-2 positive and SARS-CoV-2 negative patients were formed.

For sensitivity analyses, we further excluded patients who were chronically bedridden, admitted from a nursing home or those with a documented palliative treatment goal in order to avoid potential confounding by treatment restrictions (reduced cohort 1). A second sensitivity cohort was based on excluding patients with either missing documented respiratory rate on admission or admission from another hospital (reduced cohort 2).

Score definition and outcome parameters

The CRB-65 and qSOFA scores were calculated from the first set of parameter measurements after hospital admission as described previously [14, 15]. For better comparison, we complemented the CRB to the CRB-65 score and the qSOFA-65 to the qSOFA score by eliminating/ involving the age criterion ≥ 65 years.

Predefined outcomes were all-cause hospital mortality, mechanical ventilation (non-invasive or invasive) during the hospital stay and the combination of hospital mortality and / or mechanical ventilation.

Statistical analysis

The characteristics of the patients are represented as absolute and relative frequencies or as median with first and third quartiles (Q1, Q3). For univariable analyses, continuous variables were compared using the Mann-Whitney U-test and categorical variables using the Fisher's

exact test. Multivariable results are based on Poisson regressions with a log link function. In the primary multivariable model, we included the CRB-65 and qSOFA criteria as independent variables. The results are represented as risk ratios (RR) with 95% confidence intervals. To evaluate diagnostic qualities, we used area under the curve (AUC), sensitivity, specificity, positive/negative predictive value (PPV/ NPV) and positive/negative likelihood ratios with their 95% CI. For sensitivity analyses we added an extended multivariable model which includes the variables sex, admission from nursing home, chronically bedridden and palliative treatment goal.

We applied a two-sided significance level of 0.05. For the statistical analyses, we used R (version 3.6.2) and the R package pROC.

Results

Patient characteristics and outcomes

Overall, 280,100 patients with CAP were included in the database in 2020. After application of the predefined exclusion criteria, 167,880 (71%) SARS-CoV-2 negative and 68,594 (29%) SARS-CoV-2 positive CAP cases were left in the main cohort (figure 1). For sensitivity analyses, we excluded further 74,422 patients chronically bedridden, living in a nursing home or with a documented palliative treatment goal (reduced cohort 1) and 15,428 patients with no documented respiratory rate or admission from another hospital (reduced cohort 2).

When comparing SARS-CoV-2 positive and negative CAP in the main cohort, hospital mortality was 22.7% (n= 15,540/ 68,594) in SARS-CoV-2 positive and 15.7% (n= 26,309/ 167,880; p<0,001) in SARS-CoV-2 negative patients (supplementary table S1). Mechanical ventilation rate was 14.9% (n= 10,198/ 68,594) in SARS-CoV-2 positive vs. 9.2% (n= 15,587/ 167,880; p<0,001) in SARS-CoV-2 negative patients. Of SARS-CoV-2 positive patients with mechanical ventilation, 5336 (52%) received only non-invasive, 1974 (19%) only invasive and 2888 (28%) both non-invasive and invasive ventilation. After excluding frail or palliative patients (reduced cohort 1), both hospital mortality and ventilation rate decreased in both groups but remained significantly higher in the SARS-CoV-2 group (hospital mortality 8.8% vs 6.1%; p<0,001; ventilation rate 14% vs 8.3%; p<0,001) (supplementary tables S2, S3). Demographic data and score parameters of the main cohort of SARS-CoV-2 cases are provided in table 1 and those of CAP without SARS-CoV-2 infection in the supplementary table S4.

Score prediction in the main cohort

All criteria of the CRB-65 and qSOFA scores were associated with the prognosis of SARS-CoV-2 positive CAP in both univariable and multivariable analyses (tables 1 and 2). The corresponding values are shown in bar charts in the supplementary figure S1. With a risk ratio (RR) of 9.3 (8.7-10), age was the strongest predictor for hospital mortality, while respiratory rate was the strongest predictor for mechanical ventilation (RR 1.7; 1.6-1.8) after multivariable analyses.

Prognostic performance measures of the scores to predict hospital mortality or mechanical ventilation in SARS-CoV-2 positive CAP are depicted in tables 3 and 4, respectively. While the CRB-65 provided better prognostic accuracy in predicting mortality than the qSOFA (AUC 0.76 [0.76-0.77] vs. 0.65 [0.64-0.65]), after including the age criterion to the qSOFA, the resulting qSOFA-65 score provided a similar accuracy (AUC 0.76 [0.75-0.76]). For scores without the age criterion, NPVs for qSOFA/CRB=0 were only 83.5% and 84.7% for mortality prediction, respectively. Only the inclusion of age enabled high negative prediction concerning mortality (NPVs >97%).

When comparing mortality prediction of the SARS-CoV-2 positive with the SARS-CoV-2 negative cohort, prognostic accuracies of the scores including the age criterion were higher in SARS-CoV-2 positive CAP (AUC SARS-CoV-2 positive CRB-65 0.76, qSOFA 0.65, qSOFA-65 0.76 vs. AUC SARS-CoV-2 negative CRB-65 0.68, qSOFA 0.65, qSOFA-65 0.69, table 3 and supplementary table S5). This was associated with a higher predictive dominance of the age criterion in the SARS-CoV-2 positive (RR 9.3, table 2) compared to the SARS-CoV-2 negative cohort (RR 2.99, supplementary table S6) in multivariable analyses.

For prediction of mechanical ventilation, while all single score parameters again were associated with the outcome, prognostic accuracies of all scores were lower compared to mortality prediction. Among all evaluated scores, qSOFA-65 provided the best prediction with an AUC of 0.62 (table 4). No score achieved sufficient NPVs as even with a qSOFA-65 of 0 requirement of mechanical ventilation would have been overseen in 8.4% or 1,490/ 17,761 patients corresponding to 15% of all patients with mechanical ventilation in the disease course. On the other hand, patients with at least one score criterion except age (CRB or qSOFA >0) had a high risk for mechanical ventilation with positive predictive values of >20%.

Performance measures of all scores for prediction of mechanical ventilation in the SARS-CoV-2 negative cohort are provided in supplementary table S7. When comparing mechanical ventilation prediction for SARS-CoV-2 positive with SARS-CoV-2 negative CAP, prognostic accuracies of scores including the age criterion were nearly similar (AUC qSOFA-65 0.62 vs.

0.61, AUC CRB-65 0.60 vs. 0.59). Higher NPVs for scores of 0 were achieved in the SARS-CoV-2 negative cohort (NPVs 93-94% vs. 88-92% in the SARS-CoV-2 positive cohort).

The corresponding values for the combined endpoint mortality and/ or mechanical ventilation in the SARS-CoV-2 positive and negative CAP cohorts are shown in the supplementary tables S8 and S9.

Sensitivity analyses (score prediction in the reduced cohorts)

After exclusion of frail and palliative patients, mortality rate in the SARS-CoV-2 infected reduced cohort 1 decreased considerably (4,512/ 51,015; 8.8%) while rates of mechanical ventilation remained high (7,119/ 51,015; 14.0%; supplementary table S2). After multivariable analyses, the relative risk of age for mortality was considerably decreased compared to the main cohort (RR 6.9 [6.2-7.5] vs. RR 9.3 [8.7-10]) (supplementary table S10). In contrast, there was no major change in the RR of the age criterion for prediction of mechanical ventilation in the reduced cohort 1 compared to the main cohort (RR 1.3 [1.2-1.3] vs. RR 1.2 [1.1-1.2]).

Overall, AUCs for all scores regarding both mortality and mechanical ventilation were similar to the results from the main cohort (e.g., CRB-65 for mortality 0.75 vs. 0.76, qSOFA 0.63 vs. 0.65) (supplementary tables S11 - S13). This also applied to the SARS-CoV-2 negative cohort (supplementary tables S14 – S16).

As expected, NPVs of all scores for mortality prediction improved after excluding patients with potential treatment limitations (e.g., qSOFA Score= 0 NPV 94.1% vs. 84.7%). Nonetheless, 5.9% (1,971/ 33,643) patients died without any positive criterion detected by the qSOFA. On the other hand, after adding the age criterion, a qSOFA-65 of 0 achieved the highest NPV of all scores with 98.8% (200/ 17,309 deceased patients “overseen”).

For mechanical ventilation prediction, also in the reduced cohort 1 no risk score was able to achieve high NPVs (risk scores= 0 with NPVs between 89% and 92%).

For the reduced cohort 2 after excluding all cases with missing respiratory rate on admission or transfer from another hospital, predictive accuracies of all scores showed nearly identical values compared to the main cohort (e.g., AUC for mortality prediction of CRB-65 0.76, for qSOFA 0.65, data on file).

Discussion

The current evaluation of established and commonly used risk scores including the CRB-65 and the qSOFA in our population-based representative cohort of all 2020 hospitalized cases

with SARS-CoV-2 positive and SARS-CoV-2 negative CAP in Germany generated the following main results:

(a) Both hospital mortality and mechanical ventilation rate were higher in SARS-CoV-2 infected compared to SARS-CoV-2 non-infected CAP patients. (b) For mortality, especially in SARS-CoV-2 positive CAP, prediction was largely dominated by the age criterion and only scores including age showed sufficient screening sensitivity. (c) Sensitivity of the qSOFA-criteria was slightly superior compared to the CRB-criteria. (d) Sensitivity for prediction of mechanical ventilation was poor with all evaluated scores, as even within the highest sensitivity constellation (qSOFA-65=0) 8% of patients required mechanical ventilation and 15% of all patients requiring mechanical ventilation would have been overseen.

The study presents real-world data of virtually all hospitalized patients with an ICD-based diagnosis of CAP with or without documented SARS-CoV-2 infection in Germany in 2020. Thus, the main strength of our analysis lies in its population based large sample avoiding the bias inherent in selected study populations. Therefore, we believe that our data are of high clinical relevance and external validity.

Patients with CAP and SARS-CoV-2 infection had a significantly higher risk of dying (22.7% vs. 15.7%) or mechanical ventilation (14.9% vs. 9.2%) compared to CAP without SARS-CoV-2 infection. Such differences also have been described by others [16, 17], however for direct comparison of CAP patients with and without SARS-CoV-2 infection hospitalized within the same period we found surprisingly few data. Mortality rate in our cohort of hospitalized CAP and COVID-19 was high compared to previous prospective studies [8, 16, 18], but closely resembled that of other European population-based cohorts for hospitalized CAP [19-21] and COVID-19 [9, 10, 12, 22]. Additionally, the median age of our cohorts was high with 72 years in SARS-CoV-2 positive and 78 years in SARS-CoV-2 negative patients, respectively. Of note, older age defined by the CRB-65 cut-off of 65 years was associated with a much higher relative mortality risk in SARS-CoV-2 positive CAP compared to SARS-CoV-2 negative CAP in multivariable analyses, underscoring the dominating prognostic relevance of age described in COVID-19 [22, 23]. On the other hand, pneumonia-related confusion showed a stronger association with mechanical ventilation and mortality in SARS-CoV-2 negative (RR 2.2 and 1.9) compared to SARS-CoV-2 positive (RR 1.5 and 1.6) patients, probably reflecting the lower rate of extra-pulmonary sepsis in patients with COVID-19 compared to bacterial CAP [16].

In the current epidemiologic situation, SARS-CoV-2 needs to be considered as one possible etiological pathogen amongst many others during clinical evaluation of patients presenting with CAP. Thus, a universally applicable risk stratification approach for CAP patients is essential. It seems questionable whether complex COVID-19-specific risk scores like the ISARIC 4C models [5, 6] represent feasible screening tools for initial all-cause CAP evaluation in busy emergency departments. By contrast, the evaluated risk scores CRB-65 and qSOFA have been widely implemented for initial CAP evaluation [7, 24], and are clinically relevant screening tools to be validated in SARS-CoV-2 positive CAP.

As described previously in SARS-CoV-2 negative CAP [20, 25], the age-criterion is necessary to provide a sensitive mortality prediction with both, the CRB- and the qSOFA-criteria also in SARS-CoV-2 positive CAP. The resulting CRB-65 and qSOFA-65 scores provided similar prognostic accuracies with an adequate NPV for hospital mortality in our SARS-CoV-2 positive cohort (AUC 0.76 and NPV 98% each). Moreover, they showed superior accuracy for prediction of hospital mortality compared to the SARS-CoV-2 negative cohort (AUC 0.68 and 0.69). When compared to previously published cohorts including >2.000 patients with SARS-CoV-2 positive CAP, our mortality prediction by the qSOFA (AUC 0.65) and the CRB-65 (AUC 0.76) was comparable (published AUC range qSOFA 0.55 – 0.63; CRB-65 0.68-0.75) [5, 8-11] with the exception of one cohort showing a higher AUC for the qSOFA of 0.73 [12]. We found no published data for the qSOFA-65 in SARS-CoV-2 positive CAP. The initially recommended qSOFA score cut off ≥ 2 [15] did not show sufficient sensitivity (15%) for hospital mortality in our cohort, as previously also demonstrated for SARS-CoV-2 negative CAP [20, 26] and sepsis [27].

For prediction of mechanical ventilation in the SARS-CoV-2 positive CAP cohort, there was no sufficient sensitivity for any evaluated risk score. With an AUC of 0.62 qSOFA-65 provided the relatively best prediction, but still would have overseen 15% of all patients requiring mechanical ventilation with the most sensitive cut-off of 0. Compared to the SARS-CoV-2 negative cohort, prognostic accuracies especially of scores without the age-criterion were even lower in SARS-CoV-2 positive patients (e.g. AUC qSOFA SARS-CoV-2 positive 0.61, negative 0.64). This supplements previous data showing poor prediction of mechanical ventilation and organ support by the qSOFA or the CRB-65 in COVID-19 [8, 10, 12]. Therefore – similar to SARS-CoV-2 negative CAP [7, 24, 28] - additional risk assessment tools seem necessary for organ failure prediction in SARS-CoV-2 positive CAP. Oxygenation measurement repeatedly has been shown to provide independent prediction of mechanical ventilation in COVID-19 [8, 23, 29, 30]. For example, a respiratory score including respiratory

rate, respiratory saturation and oxygen flow rate in one study accurately predicted early mechanical ventilation for COVID-19 when compared to the qSOFA (AUC 0.81 vs. 0.59) [30]. Additionally, current CAP-guidelines recommend the ATS/IDSA minor criteria for organ failure evaluation [7, 28], which recently also have been validated for SARS-CoV-2 positive patients [29].

The following limitations of our study should be mentioned. The interpretation of our findings is limited by the lack of data from other important outcomes such as ICU admission, septic shock or follow-up data to calculate 30-day mortality. Additionally, we cannot provide data on microbiology including co-infections, comorbidities, treatment and cause of deaths. Patients with a primary hospital discharge diagnosis of ARDS are not included in the database as the ICD-based filter for the quality assurance program does not identify them. 3.3% of cases had no documented respiratory rate on admission, which might have biased the prognostic accuracies of the scores. However, sensitivity analysis after excluding these cases did not relevantly alter the results. As measurements are performed during clinical routine and collection of the data is mandatory, data quality may not be comparable with trial data. Furthermore, the quality assurance program lacks data for calculation of additional risk scores like CURB-65, PSI, minor criteria, or data on oxygenation and COVID-specific risk scores.

We evaluated data of SARS-CoV-2-positive patients hospitalized with CAP in Germany during 2020. Whether our findings are applicable for SARS-CoV-2 positive CAP in later stages of the pandemic affected by continuous evolution of the virus, host immunity and clinical management of COVID-19, is unknown and suspect to further study.

On the other hand, the coverage of virtually all hospitalized patients with SARS-CoV-2 positive and SARS-CoV-2 negative CAP in Germany reflecting real-world management and minimizing any selection bias, and the completeness of the outcome parameters as well as the other parameters of the qSOFA and CRB-65 scores, make the evaluated database unique for evaluation of SARS-CoV-2 associated hospitalized CAP.

Conclusion

Hospital mortality and mechanical ventilation rate in Germany in 2020 was higher for patients with SARS-CoV-2 infected compared to SARS-CoV-2 non-infected hospitalized CAP. For SARS-CoV-2 positive CAP, the qSOFA had low sensitivity for hospital mortality prediction,

but scores including the age criterion like the CRB-65 or the qSOFA-65 showed an acceptable accuracy, which was even higher than that for SARS-CoV-2 negative CAP. For prediction of mechanical ventilation, all evaluated scores showed insufficient sensitivity.

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Tables:

Table 1. Characteristics of the SARS-CoV-2 positive CAP cohort. Median together with the first and third quartiles (Q1, Q3) and absolute and relative frequencies (N, %) are provided. For the comparison of the subgroups, p-values from the Fisher's exact test or the Mann-Whitney-U-Test are provided. *all p-value < 0,001

Characteristic	SARS-CoV-2 pos. mortality (N= 15,540)	SARS-CoV-2 pos. survivors (N= 53,054)	SARS-CoV-2 pos. mechanical ventilation (N= 10,198)	SARS-CoV-2 pos. non-ventilated (N= 58,396)	SARS-CoV-2 pos. mortality and/or mechanical ventilation (N= 20,528)	SARS-CoV-2 pos. survivor and non-ventilated (N= 48,066)
age, in years; median (Q1, Q3)	83 (77, 88)*	66 (53, 79)*	73 (61, 81)*	71 (56, 82)*	81 (71, 86)*	66 (53, 79)*
males; N (%)	9013 (58.0%)*	29913 (56.4%)*	6758 (66.3%)*	32168 (55.1%)*	12320 (60%)*	26606 (55.4%)*
respiratory rate at admission, in breaths/min; median (Q1, Q3)	21 (18, 26)*	18 (16, 22)*	22 (18, 27)*	19 (16, 22)*	21 (18, 26)*	18 (16, 22)*
pneumonia-associated confusion; N (%)	2326 (15.0%)*	1815 (3.4%)*	1133 (11.1%)*	3008 (5.2%)*	2662 (13.0%)*	1479 (3.1%)*
systolic blood pressure, in mmHg; median (Q1, Q3)	130 (110, 148)*	132 (120, 148)*	131 (119, 149)*	131 (120, 147)*	130 (114, 148)*	132 (120, 147)*
diastolic blood pressure, in mmHg; median (Q1, Q3)	72 (61, 81)*	80 (70, 85)*	75 (66, 84)*	78 (70, 85)*	74 (64, 83)*	80 (70, 85)*
chronically bedridden; N (%)	4061 (26.1%)*	2647 (5.0%)*	665 (6.5%)*	6043 (10.3%)*	4206 (20.5%)*	2502 (5.2%)*
admission from nursing home; N (%)	6325 (40.7%)*	5129 (9.7%)*	1211 (11.9%)*	10243 (17.5%)*	6576 (32.0%)*	4878 (10.1%)*
palliative treatment goal; N (%)	8366 (53.9%)*	1671 (3.1%)*	2307 (22.6%)*	7730 (13.3%)*	8462 (41.2%)*	1575 (3.3%)*
CRB-65 score; median (Q1, Q3)	1 (1, 2)*	1 (0, 1)*	1 (1, 2)*	1 (0, 1)*	1 (1, 2)*	1 (0, 1)*
CRB score; median (Q1, Q3)	0 (0, 1)*	0 (0, 0)*	0 (0, 1)*	0 (0, 0)*	0 (0, 1)*	0 (0, 0)*
itemized:						
confusion (C); N (%)	2326 (15.0%)*	1815 (3.4%)*	1133 (11.1%)*	3008 (5.2%)*	2662 (13.0%)*	1479 (3.1%)*
respiratory rate at admission ≥ 30 breaths/min (R); N (%)	2563 (16.5%)*	2975 (5.6%)*	1882 (18.5%)*	3656 (6.3%)*	3337 (16.3%)*	2201 (4.6%)*
systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg (B); N (%)	3900 (25.1%)*	5738 (10.8%)*	1895 (18.6%)*	7743 (13.3%)*	4558 (22.2%)*	5080 (10.6%)*
age ≥ 65; N (%)	14681 (94.5%)*	27557 (51.9%)*	6949 (68.1%)*	35289 (60.4%)*	17049 (83.1%)*	25189 (52.4%)*
qSOFA-65 score; median (Q1, Q3)	2 (1, 2)*	1 (0, 1)*	1 (1, 2)*	1 (0, 1)*	1 (1, 2)*	1 (0, 1)*
qSOFA Score; median (Q1, Q3)	1 (0, 1)*	0 (0, 1)*	1 (1, 2)*	0 (0, 1)*	1 (0, 1)*	0 (0, 1)*
itemized (for items different from CRB-65):						
respiratory rate at admission ≥ 22 breaths/min; N (%)	7305 (47.0%)*	14873 (28.0%)*	5068 (49.7%)*	17110 (29.3%)*	9571 (46.6%)*	12607 (26.2%)*
systolic blood pressure ≤ 100 mmHg; N (%)	2202 (14.2%)*	2513 (4.7%)*	902 (8.8%)*	3813 (6.5%)*	2495 (12.2%)*	2220 (4.6%)*

Table 2. Multivariable analyses for hospital mortality, need for mechanical ventilation and combined endpoints hospital mortality and/ or mechanical ventilation for the SARS-CoV-2 positive main cohort. Risk ratio (RR) together with the 95% confidence interval (95% CI) and the corresponding p-value are provided. The results are based on Poisson regression modelling.

	SARS-CoV-2 pos. Mortality		SARS-CoV-2 pos. mechanical ventilation		SARS-CoV-2 pos. mortality and/ or mechanical ventilation	
	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Primary multivariable model						
CRB-65 Score						
confusion (C)	1.60 (1.52, 1.67)	<0.001	1.48 (1.38, 1.58)	<0.001	1.52 (1.46, 1.59)	<0.001
respiratory rate at admission \geq 30 breaths/min (R)	1.41 (1.34, 1.48)	<0.001	1.70 (1.60, 1.80)	<0.001	1.45 (1.39, 1.52)	<0.001
systolic blood pressure < 90 or diastolic blood pressure \leq 60 mmHg (B)	1.32 (1.26, 1.38)	<0.001	1.22 (1.15, 1.29)	<0.001	1.26 (1.21, 1.31)	<0.001
age \geq 65 years (65)	9.31 (8.69, 10.00)	<0.001	1.18 (1.13, 1.23)	<0.001	2.70 (2.60, 2.80)	<0.001
qSOFA						
respiratory rate at admission \geq 22 breaths/min	1.47 (1.41, 1.52)	<0.001	1.73 (1.65, 1.81)	<0.001	1.50 (1.45, 1.55)	<0.001
systolic blood pressure \leq 100 mmHg	1.36 (1.29, 1.44)	<0.001	0.94 (0.86, 1.01)	0.10	1.25 (1.19, 1.32)	<0.001
Extended multivariable model						
CRB-65 Score						
confusion (C)	1.31 (1.25, 1.37)	<0.001	1.43 (1.34, 1.53)	<0.001	1.31 (1.25, 1.37)	<0.001
respiratory rate at admission \geq 30 breaths/min (R)	1.23 (1.17, 1.29)	<0.001	1.67 (1.57, 1.76)	<0.001	1.31 (1.26, 1.37)	<0.001
systolic blood pressure < 90 or diastolic blood pressure \leq 60 mmHg (B)	1.20 (1.15, 1.25)	<0.001	1.26 (1.19, 1.34)	<0.001	1.18 (1.14, 1.23)	<0.001
age \geq 65 years (65)	5.71 (5.32, 6.15)	<0.001	1.26 (1.20, 1.32)	<0.001	1.95 (1.88, 2.03)	<0.001
qSOFA						
respiratory rate at admission \geq 22 breaths/min	1.29 (1.24, 1.34)	<0.001	1.72 (1.64, 1.80)	<0.001	1.38 (1.33, 1.42)	<0.001
systolic blood pressure \leq 100 mmHg	1.10 (1.04, 1.17)	<0.001	1.00 (0.92, 1.08)	0.98	1.08 (1.02, 1.13)	<0.001
male sex	1.23 (1.19, 1.27)	<0.001	1.41 (1.36, 1.47)	<0.001	1.25 (1.21, 1.29)	<0.001
admission from nursing home	1.29 (1.24, 1.34)	<0.001	0.53 (0.49, 0.56)	<0.001	1.15 (1.11, 1.19)	<0.001
chronically bedridden	1.16 (1.12, 1.21)	<0.001	0.60 (0.55, 0.66)	<0.001	1.13 (1.08, 1.18)	<0.001
palliative treatment goal	3.54 (3.41, 3.67)	<0.001	1.69 (1.60, 1.79)	<0.001	2.65 (2.57, 2.74)	<0.001

Table 3. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of hospital mortality in the SARS-CoV-2 positive main cohort. Number of cases are provided together with absolute and relative frequencies (n, %) of died patients.

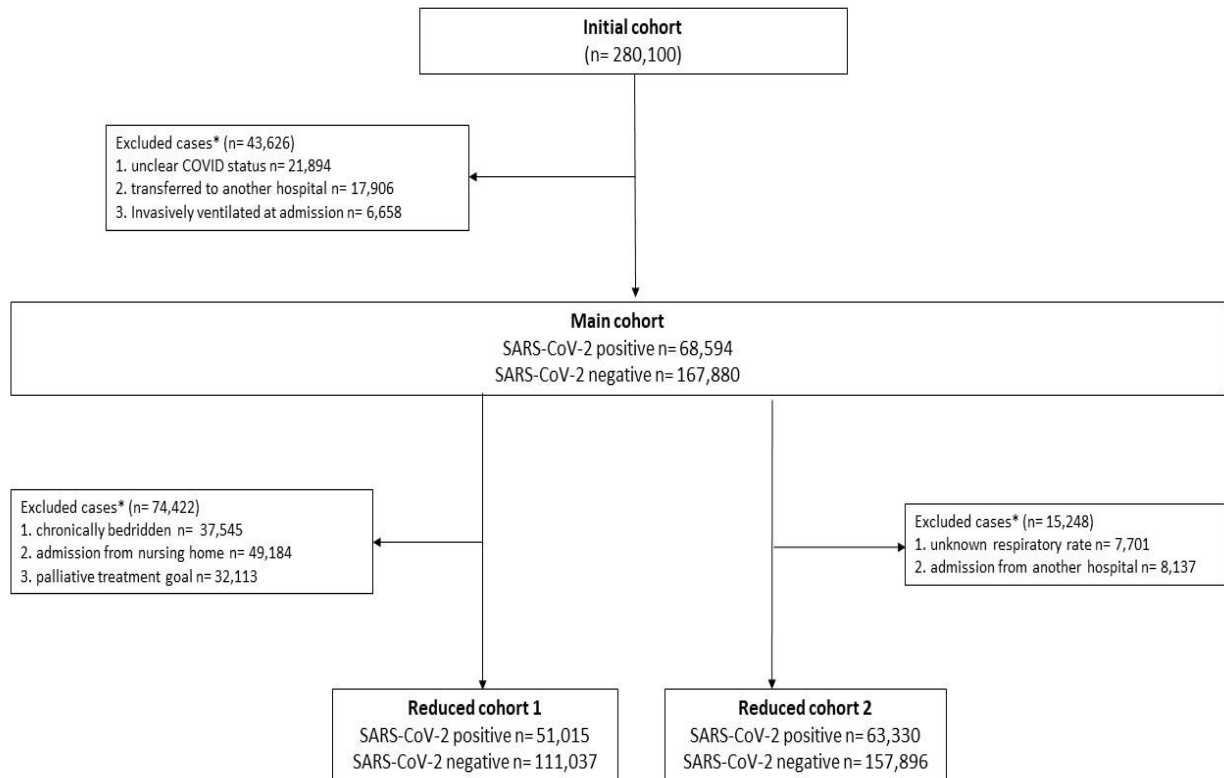
Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	15540/ 68594 (22.7%)	-	100 (100, 100)	0 (0, 0)	22.7 (22.3, 23.0)	-	1.00	-	0.64 (0.63, 0.64)
≥ 1	6945/ 16655 (41.7%)	8595/ 51939 (16.6%)	44.7 (44.2, 45.5)	81.7 (81.4, 82.0)	41.7 (41.0, 42.4)	83.5 (83.1, 83.8)	2.44 (2.38, 2.50)	0.68 (0.67, 0.69)	
≥ 2	1623/ 2404 (67.5%)	13917/ 66190 (21.0%)	10.4 (9.5, 10.9)	98.5 (98.4, 98.6)	67.5 (65.6, 69.4)	79.0 (78.7, 79.3)	7.09 (6.55, 7.68)	0.91 (0.90, 0.91)	
3	221/ 258 (85.7%)	15319/ 68336 (22.4%)	1.4 (0.8, 1.6)	99.9 (99.9, 100)	85.7 (81.4, 89.9)	77.6 (77.2, 77.9)	20.39 (14.40, 28.87)	0.99 (0.98, 0.99)	
qSOFA									
≥ 0	15540/ 68594 (22.7%)	-	100 (100, 100)	0 (0, 0)	22.7 (22.3, 23.0)	-	1.00	-	0.65 (0.64, 0.65)
≥ 1	9131/ 26713 (34.2%)	6409/ 41881 (15.3%)	58.8 (58.0, 59.5)	66.9 (66.5, 67.3)	34.2 (33.6, 34.8)	84.7 (84.4, 85.0)	1.77 (1.74, 1.81)	0.62 (0.60, 0.63)	
≥ 2	2372/ 3918 (60.5%)	13168/ 64676 (20.4%)	15.3 (14.7, 15.8)	97.1 (96.6, 97.2)	60.5 (59.0, 62.1)	79.6 (79.3, 80.0)	5.24 (4.94, 5.56)	0.87 (0.87, 0.88)	
3	330/ 403 (81.9%)	15210/ 68191 (22.3%)	2.1 (1.9, 2.4)	99.9 (99.8, 99.9)	81.9 (78.1, 85.6)	77.7 (77.4, 78.0)	15.43 (11.98, 19.87)	0.98 (0.98, 0.98)	
CRB-65									
≥ 0	15540/ 68594 (22.7%)	-	100 (100, 100)	0 (0, 0)	22.7 (22.3, 23.0)	-	1.00	-	0.76 (0.76, 0.77)
≥ 1	15037/ 46201 (32.5%)	503/ 22393 (2.2%)	96.8 (96.5, 97.0)	41.3 (40.8, 41.7)	32.5 (32.1, 33.0)	97.6 (97.6, 98.0)	1.65 (1.63, 1.66)	0.08 (0.07, 0.09)	
≥ 2	6665/ 12993 (51.3%)	8875/ 55601 (16.0%)	42.9 (42.1, 43.7)	88.1 (87.8, 88.3)	51.3 (50.4, 52.2)	84.0 (83.7, 84.3)	3.60 (3.49, 3.70)	0.65 (0.64, 0.66)	
≥ 3	1554/ 2114 (73.5%)	13986/ 66480 (21.0%)	10.0 (9.5, 10.5)	98.9 (98.9, 99.0)	73.5 (71.3, 75.7)	79.0 (78.7, 79.3)	9.47 (8.64, 10.39)	0.91 (0.91, 0.91)	
4	214/ 247 (86.6%)	15326/ 68347 (22.4%)	1.4 (1.2, 1.6)	99.9 (99.9, 100)	86.6 (82.4, 90.9)	77.6 (77.3, 77.9)	22.14 (15.35, 31.93)	0.99 (0.98, 0.99)	
qSOFA-65									
≥ 0	15540/ 68594 (22.7%)	-	100 (100, 100)	0 (0, 0)	22.7 (22.3, 23.0)	-	1.00	-	0.76 (0.75, 0.76)
≥ 1	15223/ 50833 (29.9%)	317/ 17761 (1.8%)	98.0 (97.7, 98.2)	32.9 (32.5, 33.3)	29.9 (29.5, 30.3)	98.2 (98.0, 98.4)	1.46 (1.45, 1.47)	0.062 (0.06, 0.07)	
≥ 2	8719/ 18720 (46.6%)	6821/ 49874 (13.7%)	56.1 (55.3, 56.9)	81.1 (80.8, 81.5)	46.6 (45.9, 47.3)	86.3 (86.0, 86.6)	2.98 (2.91, 3.04)	0.54 (0.53, 0.55)	
≥ 3	2255/ 3345 (67.4%)	13285/ 65249 (20.4%)	14.5 (14.0, 15.1)	97.9 (97.8, 98.1)	67.4 (65.5, 69.3)	79.6 (79.3, 79.9)	7.06 (6.60, 7.56)	0.87 (0.87, 0.88)	
4	317/ 374 (84.8%)	15223/ 68220 (22.3%)	2.0 (1.8, 2.3)	99.9 (99.9, 99.9)	84.8 (81.1, 88.4)	77.7 (77.4, 78.0)	18.99 (14.33, 25.16)	0.98 (0.98, 0.98)	

Table 4. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of mechanical ventilation in the SARS-CoV-2 positive main cohort. Number of cases are provided together with absolute and relative frequencies (n, %) of ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	10198/ 68594 (14.9%)	-	100 (100, 100)	0 (0, 0)	14.9 (14.6, 15.1)	-	1.00	-	0.59 (0.59, 0.60)
≥ 1	3994/ 16655 (24.0%)	6204/ 51939 (11.9%)	39.2 (38.2, 40.1)	78.3 (78.0, 78.7)	24.0 (23.3, 24.6)	88.1 (87.8, 88.3)	1.81 (1.76, 1.86)	0.78 (0.77, 0.78)	
≥ 2	818/ 2404 (34.0%)	9380/ 66190 (14.2%)	8.0 (7.5, 8.5)	97.3 (97.2, 97.4)	34.0 (32.1, 35.9)	85.8 (85.6, 86.1)	2.96 (2.74, 3.19)	0.95 (0.94, 0.95)	
3	98/ 258 (38.0%)	10100/ 68336 (14.8%)	1.0 (0.8, 1.2)	99.7 (99.7, 99.8)	38.0 (32.1, 43.9)	85.2 (85.0, 85.5)	3.51 (2.73, 4.51)	0.99 (0.99, 1.00)	
qSOFA									
≥ 0	10198/ 68594 (14.9%)	-	100 (100, 100)	0 (0, 0)	14.9 (14.6, 15.1)	-	1.00	-	0.61 (0.61, 0.62)
≥ 1	5842/ 26713 (21.9%)	4356/ 41881 (10.4%)	57.3 (56.3, 58.2)	64.3 (63.9, 64.6)	21.9 (21.4, 22.4)	89.6 (89.3, 89.9)	1.60 (1.57, 1.64)	0.66 (0.66, 0.67)	
≥ 2	1140/ 3918 (29.1%)	9058/ 64676 (14.0%)	11.2 (10.6, 11.8)	95.2 (95.1, 95.4)	29.1 (27.7, 30.5)	86.0 (85.7, 86.3)	2.35 (2.21, 2.50)	0.93 (0.93, 0.94)	
3	121/ 403 (30.0%)	10077/ 68191 (14.8%)	1.2 (1.0, 1.4)	99.5 (99.5, 99.6)	30.0 (25.5, 34.5)	85.2 (85.0, 85.5)	2.46 (1.99, 3.04)	0.99 (0.99, 1.00)	
CRB-65									
≥ 0	10198/ 68594 (14.9%)	-	100 (100, 100)	0 (0, 0)	14.9 (14.6, 15.1)	-	1.00	-	0.60 (0.59, 0.61)
≥ 1	7959/ 46201 (17.2%)	2239/ 22393 (10.0%)	78.0 (77.2, 78.8)	34.5 (34.1, 34.9)	17.2 (16.9, 17.6)	90.0 (89.6, 90.4)	1.19 (1.18, 1.21)	0.64 (0.61, 0.66)	
≥ 2	3139/ 12993 (24.2%)	7059/ 55601 (12.7%)	30.8 (29.9, 31.7)	83.1 (82.8, 83.4)	24.2 (23.4, 24.9)	87.3 (87.0, 87.6)	1.82 (1.76, 1.89)	0.83 (0.82, 0.84)	
≥ 3	672/ 2114 (31.8%)	9526/ 66480 (14.3%)	6.6 (6.1, 7.1)	97.5 (97.4, 97.7)	31.8 (28.6, 35.0)	85.7 (85.4, 85.9)	2.67 (2.45, 2.90)	0.96 (0.95, 0.96)	
4	89/ 247 (36.0%)	10109/ 68347 (14.8%)	0.9 (0.7, 1.1)	99.7 (99.7, 99.8)	36.0 (30.0, 42.0)	85.2 (85.0, 85.5)	3.23 (2.49, 4.18)	0.99 (0.99, 1.00)	
qSOFA-65									
≥ 0	10198/ 68594 (14.9%)	-	100 (100, 100)	0 (0, 0)	14.9 (14.6, 15.1)	-	1.00	-	0.62 (0.61, 0.62)
≥ 1	8708/ 50833 (17.1%)	1490/ 17761 (8.4%)	85.4 (84.7, 86.1)	27.9 (27.5, 28.2)	17.1 (16.8, 17.5)	91.6 (91.2, 92.0)	1.18 (1.17, 1.19)	0.52 (0.50, 0.55)	
≥ 2	4314/ 18720 (23.0%)	5884/ 49874 (11.8%)	42.3 (41.3, 43.3)	75.3 (75.0, 75.7)	23.0 (22.4, 23.6)	88.2 (87.9, 88.5)	1.71 (1.67, 1.76)	0.77 (0.75, 0.78)	
≥ 3	927/ 3345 (27.7%)	9271/ 65249 (14.2%)	9.1 (8.5, 9.6)	95.9 (95.7, 96.0)	27.7 (25.2, 30.2)	85.8 (85.5, 86.1)	2.20 (2.05, 2.35)	0.95 (0.94, 0.95)	
4	103/ 374 (27.5%)	10095/ 68220 (14.8%)	1.0 (0.8, 1.2)	99.5 (99.5, 99.6)	27.5 (23.0, 32.1)	85.2 (85.0, 85.5)	2.18 (1.74, 2.73)	0.99 (0.99, 1.00)	

Figure legend

Figure 1. Flowchart. `Initial cohort` comprises all in-patient cases with community-acquired pneumonia (CAP) in year 2020. Asterisk (*) indicated that multiple reasons for exclusion per case are possible.



Flowchart. `Initial cohort` comprises all in-patient cases with community-acquired pneumonia (CAP) in year 2020. Asterisk (*) indicated that multiple reasons for exclusion per case are possible.

Supplementary material

Validation of the qSOFA and CRB-65 in SARS-CoV-2 infected community-acquired pneumonia

Tina Richter, Falko Tesch, Jochen Schmitt, Dirk Koschel, Martin Kolditz

Online supplementary material

Table S1. Comparison of characteristics in SARS-CoV-2 positive and negative CAP (community-acquired pneumonia) cases in the main cohort (after excluding unclear COVID status, transferred to another hospital and invasively ventilation on admission). Median together with the first and third quartiles (Q1, Q3) and absolute and relative frequencies (N, %), respectively, are provided. For the comparison of the two subgroups, p-values from the Mann-Whitney-U-test and Fisher's exact test, respectively, are provided. * all p-value < 0,001

Characteristic	SARS-CoV-2 positive CAP (N= 68,594)	SARS-CoV-2 negative CAP (N= 167,880)
hospital mortality; N (%)	15,540 (22.7%)*	26,309 (15.7%)*
ventilation rate; N (%)	10,198 (14.9%)*	15,587 (9.2%)*
age, in years; median (Q1, Q3)	72 (57, 82)*	78 (66, 85)*
males; N (%)	38,926 (56.7%)*	98,207 (58.5%)*
respiratory rate at admission, in breaths/min; median (Q1, Q3)	19 (16, 23)*	19 (16, 23)*
pneumonia-associated confusion; N (%)	4141 (16.0%)*	13,631 (8.1%)*
systolic blood pressure, in mmHg; median (Q1, Q3)	131 (120, 148)*	130 (115, 150)*
diastolic blood pressure, in mmHg; median (Q1, Q3)	78 (70, 85)*	75 (65, 85)*
chronically bedridden; N (%)	6708 (9.8%)*	30,837 (18.4%)*
admission from nursing home; N (%)	11,454 (16.7%)*	37,730 (22.5%)*
palliative treatment goal; N (%)	10,037 (14.6%)*	22,076 (13.1%)*
CRB-65 score; median (Q1, Q3)	1 (0, 1)*	1 (1, 2)*
CRB score; median (Q1, Q3)	0 (0, 0)*	0 (0, 1)*
itemized:		
confusion (C); N (%)	4141 (16.0%)*	13,631 (8.1%)*
respiratory rate at admission \geq 30 breaths/min (R); N (%)	5538 (8.1%)*	13,416 (8.0%)*
systolic blood pressure < 90 mmHg or diastolic blood pressure \leq 60 mmHg (B); N (%)	9638 (14.1%)*	33,169 (19.8%)*
age \geq 65; N (%)	42,238 (61.6%)*	129,433 (77.1%)*
qSOFA-65 score; median (Q1, Q3)	1 (0, 2)*	1 (1, 2)*
qSOFA Score; median (Q1, Q3)	0 (0, 0)*	0 (0, 0)*
itemized (for items different from CRB-65):		
respiratory rate at admission \geq 22 breaths/min; N (%)	22,178 (32.3%)*	53,631 (31.9%)*
systolic blood pressure \leq 100 mmHg; N (%)	4715 (6.9%)*	18,839 (11.2%)*

Table S2. Characteristics of SARS-CoV-2 positive reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Median together with the first and third quartiles (Q1, Q3) and absolute and relative frequencies (N, %) are provided. For the comparison of the subgroups, p-values from the Fisher's exact test or the Mann-Whitney-U-Test are provided. * p-value < 0,001; ** p-value < 0,5

Characteristic	SARS-CoV-2 pos. mortality	SARS-CoV-2 pos. survivors	SARS-CoV-2 pos. mechanical ventilation	SARS-CoV-2 pos. non-ventilated	SARS-CoV-2 pos. mortality and/ or mechanical ventilation	SARS-CoV-2 pos. survivor and non-ventilated
	(N= 4,512)	(N= 46,503)	(N= 7,119)	(N= 43,896)	(N= 9,135)	(N= 41,880)
age, in years; median (Q1, Q3)	80 (72, 85)*	63 (52, 76)*	68 (57, 78)*	64 (52, 77)*	73 (60, 81)*	63 (52, 76)*
males; N (%)	2,999 (66.5%)*	27,167 (58.4%)*	4,864 (68.3%)*	25,302 (57.6%)*	6,107 (66.9%)*	24,059 (57.4%)*
respiratory rate at admission, in breaths/min; median (Q1, Q3)	21 (18, 26)*	18 (16, 22)*	21 (18, 26)*	18 (16, 22)*	21 (18, 26)*	18 (16, 22)*
pneumonia-associated confusion; N (%)	582 (12.9%)*	1,329 (2.9%)*	615 (8.6%)*	1,296 (3.0%)*	877 (9.6%)*	1,034 (2.5%)*
systolic blood pressure, in mmHg; median (Q1, Q3)	132 (117, 150)	132 (120, 147)	133 (120, 150)**	132 (120, 147)**	133 (120, 150)**	132 (120, 147)**
diastolic blood pressure, in mmHg; median (Q1, Q3)	74 (64, 82)*	80 (70,86)*	77 (68, 85)*	80 (70, 85)*	76 (67, 84)*	80 (70, 86)*
CRB-65 score; median (Q1, Q3)	1 (1, 2)*	1 (0, 1)*	1 (0, 1)*	1 (0, 1)*	1 (1, 2)*	1 (0, 1)*
CRB score; median (Q1, Q3)	0 (0, 1)*	0 (0, 0)*	0 (0, 1)*	0 (0, 0)*	0 (0, 1)*	0 (0, 0)*
itemized:						
confusion (C); N (%)	582 (12.9%)*	1,329 (2.9%)*	615 (8.6%)*	1,296 (3.0%)*	877 (9.6%)*	1,034 (2.5%)*
respiratory rate at admission ≥ 30 breaths/min (R); N (%)	738 (16.4%)*	2,545 (5.5%)*	1,225 (17.2%)*	2,058 (4.7%)*	1,447 (15.8%)*	1,836 (4.4%)*
systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg (B); N (%)	981 (21.7%)*	4,505 (9.7%)*	1,150 (16.2%)*	4336 (9.9%)*	1,568 (17.2%)*	3,918 (9.4%)*
age ≥ 65; N (%)	3,994 (88.5%)*	21,617 (46.5%)*	4,142 (58.2%)*	21,469 (48.9%)*	6,086 (66.6%)*	19,525 (46.6%)*
qSOFA-65 score; median (Q1, Q3)	2 (1, 2)*	1 (0, 1)*	1 (1, 2)*	1 (0, 1)*	1 (1, 2)*	1 (0, 1)*
qSOFA Score; median (Q1, Q3)	1 (0, 1)*	0 (0, 1)*	1 (0, 1)*	0 (0, 1)*	1 (0, 1)*	0 (0, 1)*
itemized (for items different from CRB-65):						
respiratory rate at admission ≥ 22 breaths/min; N (%)	2,108 (46.7%)*	12,780 (27.5%)*	3,437 (48.3%)*	11,451 (26.1%)*	4,200 (46.0%)*	10,688 (25.5%)*
systolic blood pressure ≤ 100 mmHg; N (%)	471 (10.4%)*	1,886 (4.1%)*	496 (7.0%)*	1861 (4.2%)*	722 (7.9%)*	1635 (3.9%)*

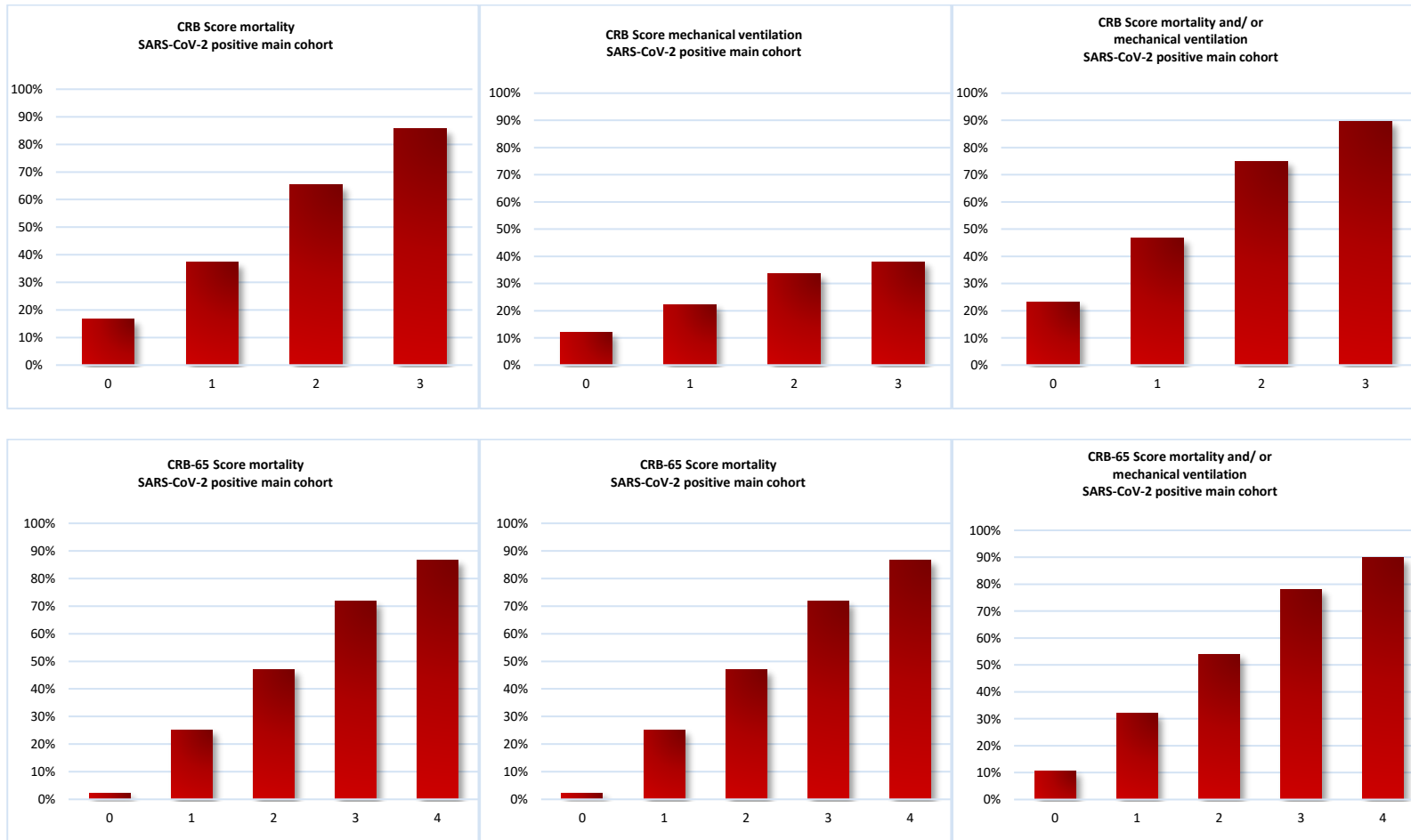
Table S3. Characteristics of SARS-CoV-2 negative reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Median together with the first and third quartiles (Q1, Q3) and absolute and relative frequencies (N, %) are provided. For the comparison of the subgroups, p-values from the Fisher’s exact test or the Mann-Whitney-U-Test are provided. * p-value < 0,001

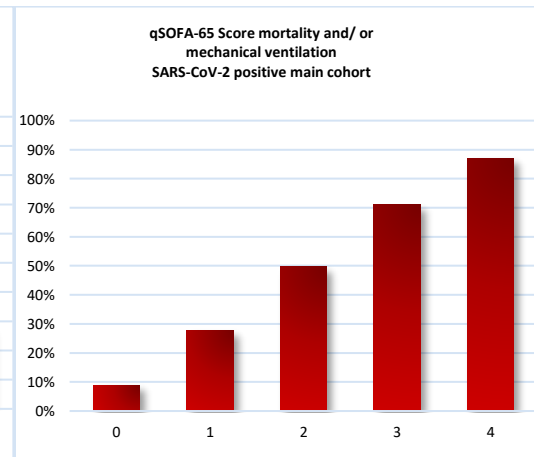
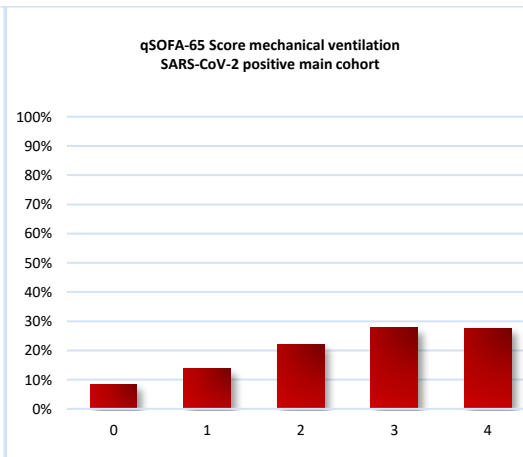
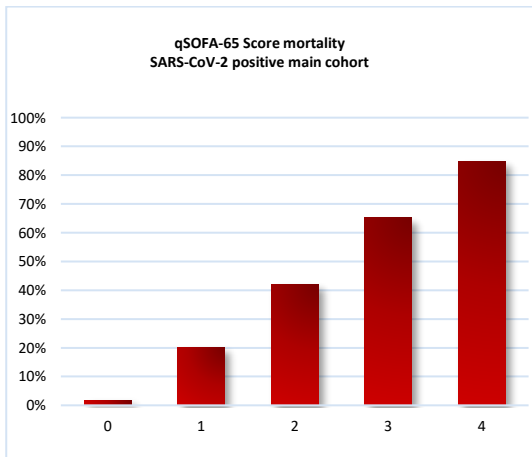
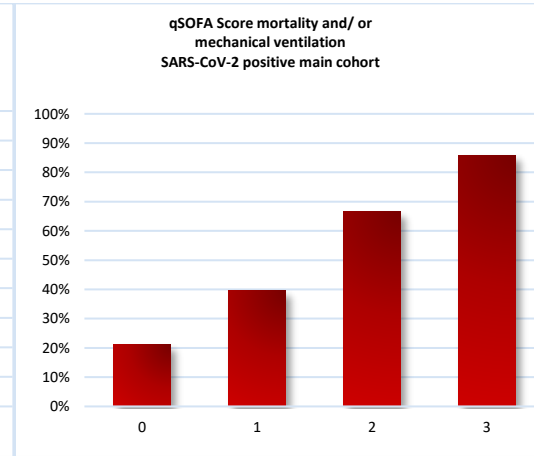
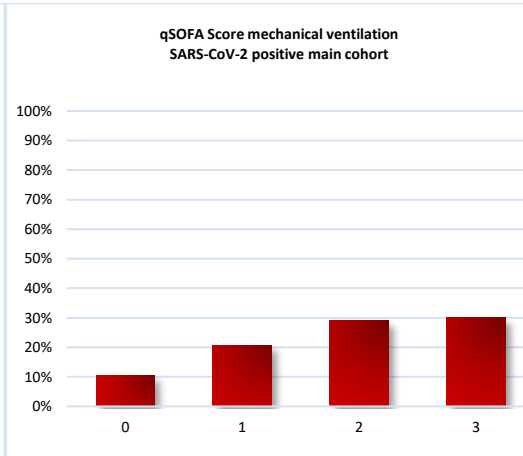
Characteristic	SARS-CoV-2 neg. mortality (N= 6,766)	SARS-CoV-2 neg. survivors (N= 104,271)	SARS-CoV-2 neg. mechanical ventilation (N= 9,214)	SARS-CoV-2 neg. non-ventilated (N= 101,823)	SARS-CoV-2 neg. mortality and/ or mechanical ventilation (N= 13,339)	SARS-CoV-2 neg. survivors and non-ventilated (N= 97,698)
age, in years; median (Q1, Q3)	80 (72, 86)*	74 (61, 82)*	72 (62, 82)*	75 (62, 83)*	76 (66, 83)*	75 (61, 82)*
males; N (%)	4,419 (65.3%)*	61,980 (59.4%)*	5,776 (62.7%)*	60,623 (59.5%)*	8,404 (63.0%)*	57,995 (59.4%)*
respiratory rate at admission, in breaths/min; median (Q1, Q3)	20 (17, 25)*	18 (16, 22)*	22 (18, 27)*	18 (16, 22)*	21 (17, 26)*	18 (16, 22)*
pneumonia-associated confusion; N (%)	1,128 (16.7%)*	5,209 (5.0%)*	1,484 (16.1%)*	4,853 (4.8%)*	2,057 (15.4%)*	4,280 (4.4%)*
systolic blood pressure, in mmHg; median (Q1, Q3)	125 (106, 144)*	135 (120, 150)*	130 (110, 150)*	135 (120, 150)*	130 (110, 149)*	135 (120, 150)*
diastolic blood pressure, in mmHg; median (Q1, Q3)	70 (60, 80)*	77 (68, 85)*	74 (62, 85)*	77 (68, 85)*	73 (60, 84)*	78 (69, 85)*
CRB-65 score; median (Q1, Q3)	1 (1, 2)*	1 (0, 1)*	1 (1, 2)*	1 (1, 1)*	1 (1, 2)*	1 (0, 1)*
CRB score; median (Q1, Q3)	0 (0, 1)*	0 (0, 0)*	0 (0, 1)*	0 (0, 0)*	0 (0, 1)*	0 (0, 0)*
itemized:						
confusion (C); N (%)	1,128 (16.7%)*	5,209 (5.0%)*	1,484 (16.1%)*	4,853 (4.8%)*	2,057 (15.4%)*	4,280 (4.4%)*
respiratory rate at admission ≥ 30 breaths/min (R); N (%)	984 (14.5%)*	57,60 (5.5%)*	1,655 (18.0%)*	5,089 (5.0%)*	2,093 (15.7%)*	4,651 (4.8%)*
systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg (B); N (%)	2,046 (30.2%)*	15,482 (14.8%)*	2,263 (24.6%)*	15,265 (15.0%)*	3,425 (25.7%)*	14,103 (14.4%)*
age ≥ 65; N (%)	5,919 (87.5%)*	72,722 (69.7%)*	6,380 (69.2%)*	72,261 (71.0%)*	10,242 (76.8%)*	68,399 (70.0%)*
qSOFA-65 score; median (Q1, Q3)	2 (1, 2)*	1 (1, 2)*	1 (1, 2)*	1 (1, 2)*	1 (1, 2)*	1 (1, 2)*
qSOFA Score; median (Q1, Q3)	1 (0, 1)*	0 (0, 1)*	1 (0, 1)*	0 (0, 1)*	1 (0, 1)*	0 (0, 1)*
itemized (for items different from CRB-65):						
respiratory rate at admission ≥ 22 breaths/min; N (%)	2,940 (43.5%)*	28,832 (27.7%)*	4,489 (48.7%)*	27,283 (26.8%)*	6,083 (45.6%)*	25,689 (26.3%)*
systolic blood pressure ≤ 100 mmHg; N (%)	1,421 (21.0%)*	7,152 (6.9%)*	1,463 (15.9%)*	7,110 (7.0%)*	2,249 (16.9%)*	6,324 (6.5%)*

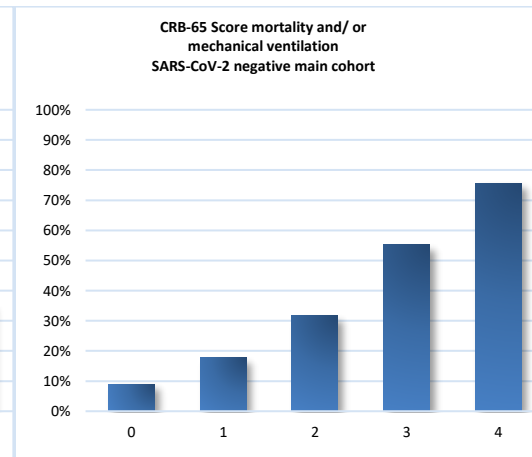
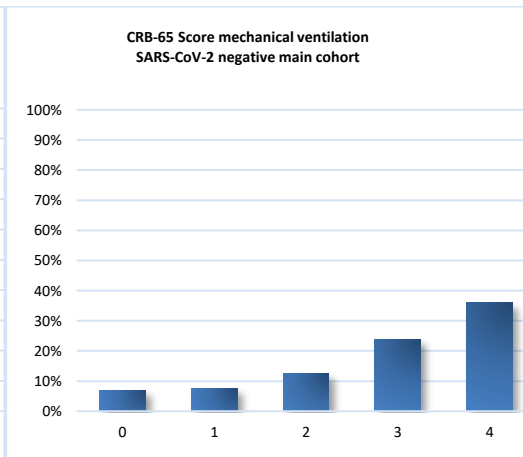
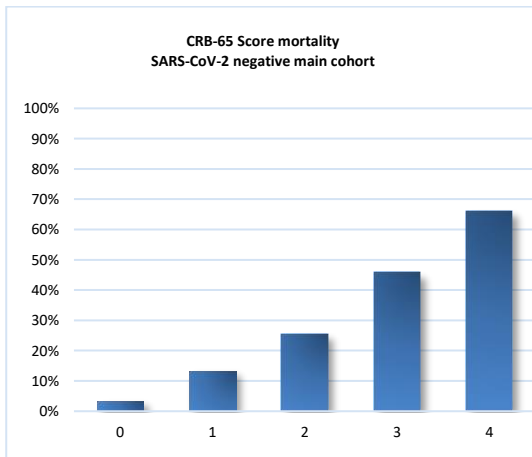
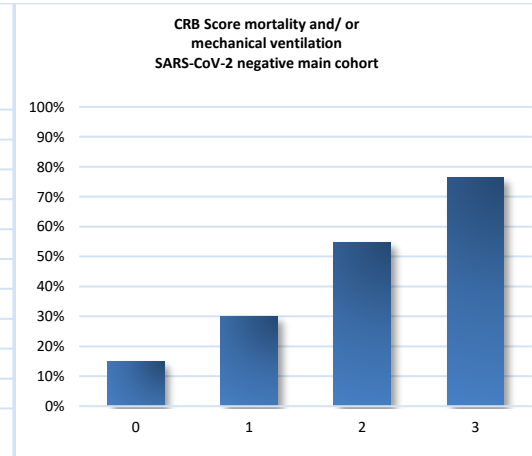
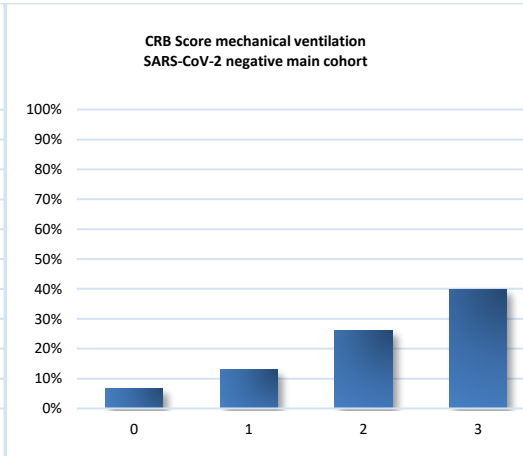
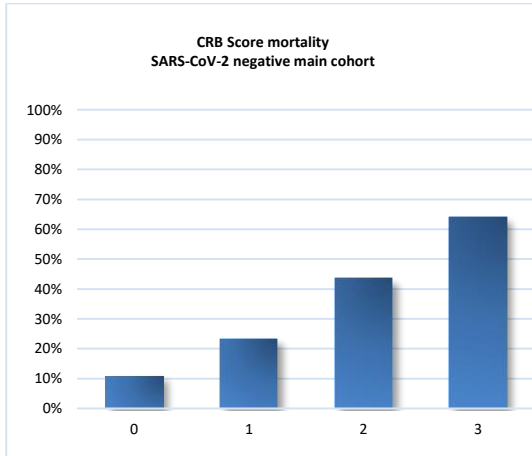
Table S4. Characteristics of SARS-CoV-2 negative CAP cohort. Median together with the first and third quartiles (Q1, Q3) and absolute and relative frequencies (N, %) are provided. For the comparison of the subgroups, p-values from the Fisher's exact test or the Mann-Whitney-U-Test are provided. *all p-value < 0,001

Characteristic	SARS-CoV-2 neg. mortality	SARS-CoV-2 neg. survivors	SARS-CoV-2 neg. mechanical ventilation	SARS-CoV-2 neg. non-ventilated	SARS-CoV-2 neg. mortality and/ or mechanical ventilation	SARS-CoV-2 neg. survivors and non-ventilated
	(N= 26,309)	(N= 141,571)	(N= 15,587)	(N= 152,293)	(N= 35,158)	(N= 132,722)
age, in years; median (Q1, Q3)	82 (76, 88)*	77 (64, 84)*	75 (64, 82)*	78 (66, 85)*	81 (71, 87)*	77 (64, 84)*
males; N (%)	15721 (59.8%)*	82486 (58.3%)*	9717 (62.3%)*	88490 (58.1%)*	21079 (60.0%)*	77128 (58.1%)*
respiratory rate at admission, in breaths/min; median (Q1, Q3)	21 (17, 26)*	18 (16, 22)*	22 (18, 28)*	18 (16, 22)*	21 (17, 26)*	18 (16, 22)*
pneumonia-associated confusion; N (%)	4930 (18.7%)*	8701 (6.1%)*	2928 (18.8%)*	10703 (7.0%)*	6264 (17.8%)*	7367 (5.6%)*
systolic blood pressure, in mmHg; median (Q1, Q3)	120 (102, 140)*	133 (118, 150)*	128 (110, 147)*	130 (116, 150)*	123 (105, 144)*	133 (119, 150)*
diastolic blood pressure, in mmHg; median (Q1, Q3)	70 (60, 80)*	76 (66, 85)*	71 (60, 83)*	75 (65, 85)*	70 (60, 81)*	76 (67, 85)*
chronically bedridden; N (%)	9799 (37.2%)*	21038 (14.9%)*	2543 (16.3%)*	28294 (18.6%)*	11101 (31.6%)*	19736 (14.9%)*
admission from nursing home; N (%)	10012 (38.1%)*	27718 (19.6%)*	2802 (18.0%)*	34928 (22.9%)*	11457 (32.6%)*	26273 (19.8%)*
palliative treatment goal; N (%)	14527 (55.2%)*	7549 (5.3%)*	3936 (25.3%)*	18140 (11.9%)*	15092 (42.9%)*	6984 (5.3%)*
CRB-65 score; median (Q1, Q3)	1 (1, 2)*	1 (1, 1)*	1 (1, 2)*	1 (1, 1)*	1 (1, 2)*	1 (1, 1)*
CRB score; median (Q1, Q3)	1 (0, 1)*	0 (0, 1)*	0 (0, 1)*	0 (0, 1)*	0 (0, 1)*	0 (0, 1)*
itemized:						
confusion (C); N (%)	4930 (18.7%)*	8701 (6.1%)*	2928 (18.8%)*	10703 (7.0%)*	6264 (17.8%)*	7367 (5.6%)*
respiratory rate at admission ≥ 30 breaths/min (R); N (%)	4327 (16.4%)*	9089 (6.4%)*	3016 (19.3%)*	10400 (6.8%)*	5878 (16.7%)*	7538 (5.7%)*
systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg (B); N (%)	8691 (33.0%)*	24478 (17.3%)*	4420 (28.4%)*	28749 (18.9%)*	10731 (30.5%)*	22438 (16.9%)*
age ≥ 65; N (%)	24138 (91.7%)*	105295 (74.4%)*	11599 (74.4%)*	117834 (77.4%)*	30135 (85.7%)*	99298 (74.8%)*
qSOFA-65 score; median (Q1, Q3)	2 (1, 2)*	1 (1, 2)*	2 (1, 2)*	1 (1, 2)*	2 (1, 2)*	1 (1, 2)*
qSOFA Score; median (Q1, Q3)	1 (0, 1)*	0 (0, 1)*	1 (0, 1)*	0 (0, 1)*	1 (0, 1)*	0 (0, 1)*
itemized (for items different from CRB-65):						
respiratory rate at admission ≥ 22 breaths/min; N (%)	12210 (46.4%)*	41421 (29.3%)*	7778 (49.9%)*	45853 (30.1%)*	16475 (46.9%)*	37156 (28.0%)*
systolic blood pressure ≤ 100 mmHg; N (%)	6380 (24.3%)*	12459 (8.8%)*	2992 (19.2%)*	15847 (10.4%)*	7654 (21.8%)*	11185 (8.4%)*

Figure S1. Bar charts of risk scores in relation to single (hospital mortality, mechanical ventilation) and combined endpoints (hospital mortality and/ or mechanical ventilation). The percentage of patients with corresponding score values is shown. Red for the SARS-CoV-2 positive patients and blue for the SARS-CoV-2 negative patients.







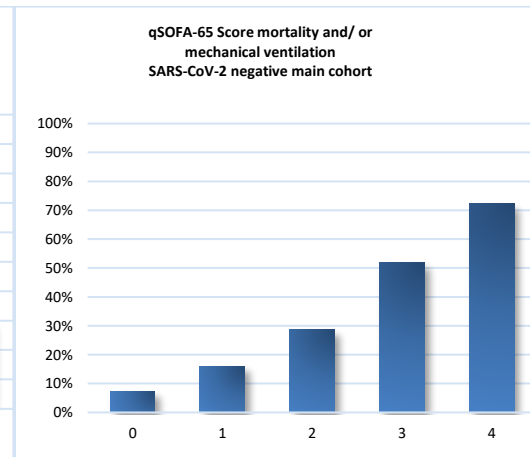
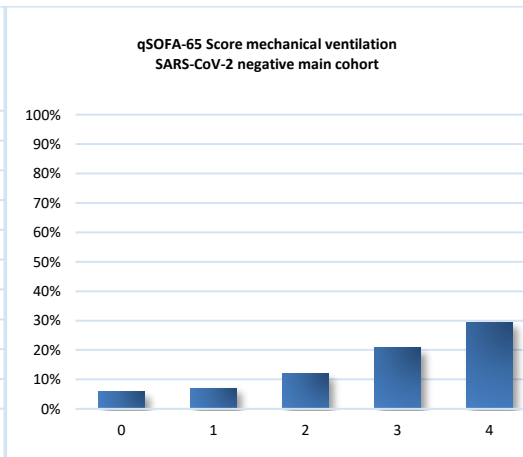
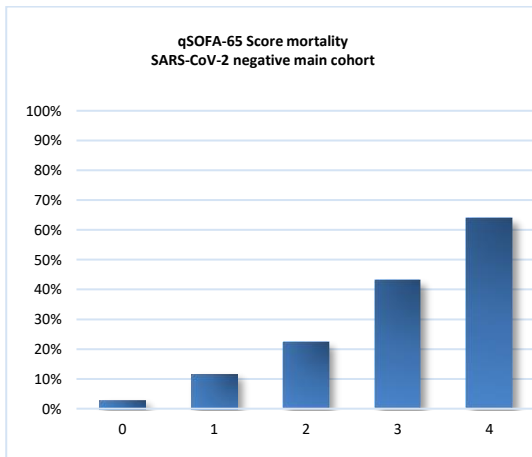
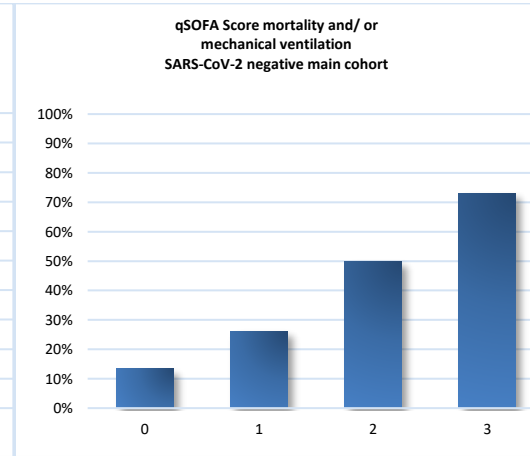
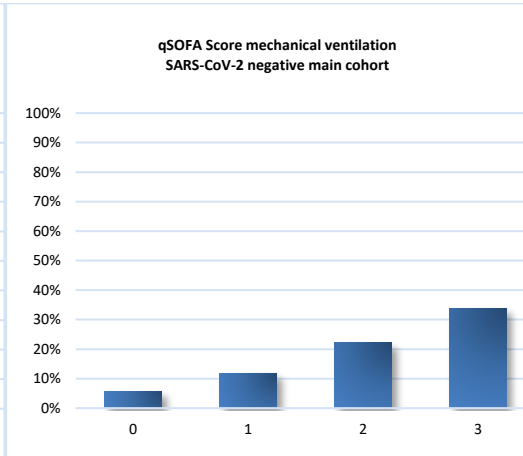
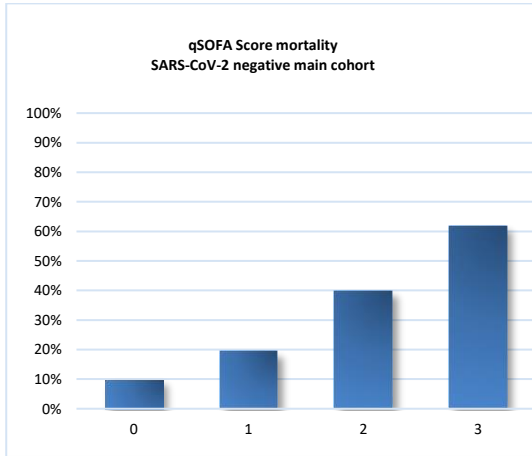


Table S5. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of hospital mortality in the SARS-CoV-2 negative main cohort. Number of cases are provided together with absolute and relative frequencies (n, %) of died patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	26309/ 167880 (15.7%)	-	100 (100, 100)	0 (0, 0)	15.7 (15.5, 15.8)	-	1.00 (1.00, 1.00)	-	0.64 (0.64, 0.64)
≥ 1	13682/ 51165 (26.7%)	12627/ 116715 (10.8%)	52.0 (51.4, 52.6)	73.5 (73.3, 73.8)	26.7 (26.4, 27.1)	89.2 (89.0, 89.4)	1.96 (1.94, 1.99)	0.65 (0.65, 0.66)	
≥ 2	3753/ 8251 (45.5%)	22556/ 159629 (14.1%)	14.3 (13.8, 14.7)	96.8 (96.7, 96.9)	45.5 (45.2, 45.8)	85.9 (85.5, 86.2)	4.49 (4.32, 4.67)	0.89 (0.88, 0.89)	
3	513/ 800 (64.1%)	25796/ 167080 (15.4%)	1.9 (1.8, 2.1)	99.8 (99.8, 99.8)	64.1 (63.4, 64.4)	84.6 (83.7, 85.4)	9.62 (8.84, 10.47)	0.98 (0.94, 1.02)	
qSOFA									
≥ 0	26309/ 167880 (15.7%)	-	100 (100, 100)	0 (0, 0)	15.7 (15.5, 15.8)	-	1.00 (1.00, 1.00)	-	0.65 (0.65, 0.66)
≥ 1	16808/ 70998 (23.7%)	9501/ 96882 (9.8%)	63.9 (63.3, 64.5)	61.7 (61.5, 62.0)	23.7 (23.4, 24.0)	90.2 (90.0, 90.4)	1.67 (1.65, 1.69)	0.59 (0.58, 0.59)	
≥ 2	5731/ 13515 (42.4%)	20578/ 154365 (13.3%)	21.8 (21.3, 22.3)	94.5 (94.4, 94.6)	42.4 (41.9, 42.9)	86.7 (86.4, 86.9)	3.96 (3.85, 4.08)	0.83 (0.82, 0.83)	
3	981/ 1588 (61.8%)	25328/ 166292 (15.2%)	3.7 (3.5, 4.0)	99.6 (99.5, 99.6)	61.8 (61.5, 62.1)	84.8 (84.1, 85.4)	8.70 (8.21, 9.22)	0.97 (0.94, 0.99)	
CRB-65									
≥ 0	26309/ 167880 (15.7%)	-	100 (100, 100)	0 (0, 0)	15.7 (15.5, 15.8)	-	1.00 (1.00, 1.00)	-	0.68 (0.68, 0.68)
≥ 1	25273/ 137475 (18.4%)	1036/ 30405 (3.4%)	96.1 (95.8, 96.3)	20.7 (20.5, 21.0)	18.4 (18.2, 18.6)	96.7 (96.4, 96.8)	1.21 (1.21, 1.22)	0.19 (0.19, 0.19)	
≥ 2	12883/ 44199 (29.1%)	13426/ 123681 (10.9%)	49.0 (48.4, 49.6)	77.9 (77.7, 78.1)	29.1 (28.7, 29.6)	89.1 (88.9, 89.3)	2.21 (2.18, 2.25)	0.66 (0.65, 0.66)	
≥ 3	3469/ 7276 (47.7%)	22840/ 160604 (14.2%)	13.2 (12.8, 13.6)	97.3 (97.2, 97.49)	47.7 (47.1, 48.2)	85.8 (85.4, 86.1)	4.90 (4.71, 5.11)	0.89 (0.89, 0.90)	
4	461/ 699 (66.0%)	25848/ 167181 (15.5%)	1.8 (1.6, 1.9)	99.8 (99.8, 99.9)	66.0 (65.7, 66.2)	84.5 (83.7, 85.4)	10.42 (9.56, 11.36)	0.98 (0.95, 1.02)	
qSOFA-65									
≥ 0	26309/ 167880 (15.7%)	-	100 (100, 100)	0 (0, 0)	15.7 (15.5, 15.8)	-	1.00 (1.00, 1.00)	-	0.69 (0.69, 0.69)
≥ 1	25626/ 143437 (17.9%)	683/ 24443 (2.8%)	97.4 (97.2, 97.6)	16.8 (16.6, 17.0)	17.9 (17.7, 18.1)	97.2 (97.0, 97.4)	1.17 (1.17, 1.17)	0.15 (0.15, 0.16)	
≥ 2	15851/ 59068 (26.8%)	10458/ 108812 (9.6%)	60.2 (59.7, 60.8)	69.5 (69.2, 69.7)	26.8 (26.5, 27.2)	90.4 (90.2, 90.6)	1.97 (1.95, 2.00)	0.57 (0.57, 0.58)	
≥ 3	5302/ 11652 (45.5%)	21007/ 156228 (13.4%)	20.2 (19.7, 20.6)	95.5 (95.4, 95.6)	45.5 (44.6, 46.4)	86.6 (86.2, 86.9)	4.49 (4.35, 4.64)	0.84 (0.83, 0.84)	
4	879/ 1377 (63.8%)	25430/ 166503 (15.3%)	3.3 (3.1, 3.6)	99.6 (99.6, 99.7)	63.8 (61.3, 66.4)	84.7 (84.0, 85.4)	9.50 (8.56, 10.54)	0.97 (0.96, 0.98)	

Table S6. Multivariable analyses for hospital mortality, need for mechanical ventilation and combined endpoints hospital mortality or/ and mechanical ventilation for the SARS-CoV-2 negative main cohort. Risk ratio (RR) together with the 95% confidence interval (95% CI) and the corresponding p-value are provided. The results are based on Poisson regression modelling.

	SARS-CoV-2 neg. mortality		SARS-CoV-2 neg. mechanical ventilation		SARS-CoV-2 neg. mortality and/ or mechanical ventilation	
	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Primary multivariable model						
CRB-65 Score						
confusion (C)	1.92 (1.85, 1.98)	0.00	2.19 (2.10, 2.29)	0.00	1.90 (1.85, 1.96)	0.00
respiratory rate at admission \geq 30 breaths/min (R)	1.45 (1.39, 1.50)	0.00	1.73 (1.65, 1.81)	0.00	1.49 (1.44, 1.54)	0.00
systolic blood pressure < 90 or diastolic blood pressure \leq 60 mmHg (B)	1.28 (1.23, 1.32)	0.00	1.26 (1.21, 1.32)	0.00	1.24 (1.20, 1.27)	0.00
age \geq 65 years (65)	2.99 (2.86, 3.13)	0.00	0.76 (0.73, 0.79)	0.00	1.60 (1.55, 1.65)	0.00
qSOFA						
respiratory rate at admission \geq 22 breaths/min	1.49 (1.45, 1.53)	0.00	1.71 (1.64, 1.77)	0.00	1.54 (1.50, 1.57)	0.00
systolic blood pressure \leq 100 mmHg	1.82 (1.76, 1.89)	0.00	1.31 (1.25, 1.38)	0.10	1.62 (1.57, 1.67)	0.00
Extended multivariable model						
CRB-65 Score						
confusion (C)	1.45 (1.41, 1.50)	0.00	2.00 (1.92, 2.09)	0.00	1.55 (1.51, 1.60)	0.00
respiratory rate at admission \geq 30 breaths/min (R)	1.18 (1.14, 1.22)	0.00	1.67 (1.60, 1.75)	0.00	1.29 (1.25, 1.33)	0.00
systolic blood pressure < 90 or diastolic blood pressure \leq 60 mmHg (B)	1.16 (1.12, 1.19)	0.00	1.26 (1.21, 1.32)	0.00	1.16 (1.12, 1.19)	0.00
age \geq 65 years (65)	2.02 (1.93, 2.12)	0.00	0.74 (0.72, 0.77)	0.00	1.24 (1.20, 1.28)	0.00
qSOFA						
respiratory rate at admission \geq 22 breaths/min	1.30 (1.27, 1.34)	0.00	1.69 (1.63, 1.75)	0.00	1.41 (1.37, 1.44)	0.00
systolic blood pressure \leq 100 mmHg	1.34 (1.30, 1.39)	0.00	1.27 (1.21, 1.34)	0.00	1.30 (1.26, 1.34)	0.00
male sex	1.08 (1.05, 1.11)	0.00	1.11 (1.07, 1.15)	0.00	1.06 (1.04, 1.08)	0.00
admission from nursing home	1.05 (1.02, 1.08)	0.00	0.65 (0.62, 0.68)	0.00	0.97 (0.95, 1.00)	0.05
chronically bedridden	1.18 (1.15, 1.22)	0.00	0.72 (0.69, 0.76)	0.00	1.14 (1.11, 1.17)	0.00
palliative treatment goal	5.90 (5.70, 6.03)	0.00	2.08 (1.99, 2.17)	0.00	3.80 (3.70, 3.89)	0.00

Table S7. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of mechanical ventilation in the SARS-CoV-2 negative main cohort. Number of cases are provided together with absolute and relative frequencies (n, %) of ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	15587/ 167880 (9.3%)	-	100 (100, 100)	0 (0, 0)	9.3 (9.1, 9.4)	-	1.00 (1.00, 1.00)	-	0.62 (0.61, 0.62)
≥ 1	7788/ 51165 (15.2%)	7799/ 116715 (6.7 %)	50.0 (49.2, 50.7)	71.5 (71.3, 71.7)	15.2 (14.9, 15.5)	93.3 (93.2, 93.5)	1.75 (1.72, 1.79)	0.70 (0.69, 0.70)	
≥ 2	2258/ 8251 (27.4%)	13329/ 159629 (8.3%)	14.5 (13.9, 15.0)	96.1 (96.0, 96.2)	27.4 (27.1, 27.6)	91.7 (91.4, 91.9)	3.68 (3.53, 3.84)	0.89 (0.88, 0.90)	
3	318/ 800 (39.8%)	15269/ 167080 (9.1%)	2.0 (1.8, 2.3)	99.7 (99.7, 99.7)	39.8 (39.5, 40.0)	90.9 (90.2, 91.5)	6.45 (5.79, 7.18)	0.98 (0.94, 1.03)	
qSOFA									
≥ 0	15587/ 167880 (9.3%)	-	100 (100, 100)	0 (0, 0)	9.3 (9.1, 9.4)	-	1.00 (1.00, 1.00)	-	0.64 (0.64, 0.64)
≥ 1	9987/ 70998 (14.1%)	5600/ 96882 (5.8%)	64.1 (63.3, 64.8)	59.9 (59.7, 60.2)	14.1 (13.8, 14.3)	94.2 (94.1, 94.4)	1.60 (1.58, 1.62)	0.60 (0.59, 0.60)	
≥ 2	3174/ 13515 (23.5%)	12413/ 154365 (8.0%)	20.4 (19.7, 21.0)	93.2 (93.1, 93.3)	23.5 (23.1, 23.9)	91.6 (91.7, 92.2)	3.00 (2.90, 3.10)	0.85 (0.85, 0.86)	
3	537/ 1588 (33.8%)	15050/ 166292 (9.1%)	3.4 (3.2, 3.7)	99.3 (99.3, 99.4)	33.6 (33.5, 34.1)	90.9 (90.4, 91.5)	4.99 (4.61, 5.41)	0.97 (0.95, 1.00)	
CRB-65									
≥ 0	15587/ 167880 (9.3%)	-	100 (100, 100)	0 (0, 0)	9.3 (9.1, 9.4)	-	1.00 (1.00, 1.00)	-	0.59 (0.59, 0.60)
≥ 1	13449/ 137475 (9.8%)	2138/ 30405 (7.0%)	86.3 (85.7, 86.8)	18.6 (18.4, 18.8)	9.8 (9.6, 9.9)	93.0 (92.7, 93.3)	1.06 (1.05, 1.07)	0.74 (0.73, 0.75)	
≥ 2	6440/ 44199 (14.6%)	9147/ 123681 (7.4%)	41.3 (40.5, 42.1)	75.2 (75.0, 75.4)	14.6 (14.2, 14.9)	92.6 (92.4, 92.8)	1.67 (1.63, 1.70)	0.78 (0.77, 0.79)	
≥ 3	1823/ 7276 (25.1%)	13764/ 160604 (8.6%)	11.7 (11.2, 12.2)	96.4 (96.3, 96.5)	25.1 (24.6, 25.5)	91.4 (91.1, 91.7)	3.27 (3.12, 3.42)	0.92 (0.90, 0.92)	
4	251/ 699 (35.9%)	15336/ 167181 (9.2%)	1.6 (1.4, 1.8)	99.7 (99.7, 99.7)	35.9 (35.6, 36.2)	90.8 (90.1, 91.5)	5.47 (4.86, 6.17)	0.99 (0.95, 1.03)	
qSOFA-65									
≥ 0	15587/ 167880 (9.3%)	-	100 (100, 100)	0 (0, 0)	9.3 (9.1, 9.4)	-	1.00 (1.00, 1.00)	-	0.61 (0.61, 0.62)
≥ 1	14159/ 143437 (9.9%)	1428/ 24443 (5.8%)	90.8 (90.4, 91.3)	15.1 (14.9, 15.3)	9.9 (9.7, 10.0)	94.1 (93.9, 94.5)	1.07 (1.07, 1.08)	0.61 (0.59, 0.62)	
≥ 2	8194/ 59068 (13.9%)	7393/ 108812 (6.8%)	52.6 (51.8, 53.4)	66.6 (66.4, 66.8)	13.9 (13.6, 14.2)	93.2 (93.0, 93.4)	1.57 (1.55, 1.60)	0.71 (0.71, 0.72)	
≥ 3	2538/ 11652 (21.8%)	13049/ 156228 (8.4%)	16.3 (15.7, 16.9)	94.0 (93.9, 94.1)	21.8 (21.03, 22.53)	91.6 (91.4, 91.9)	2.72 (2.62, 2.82)	0.89 (0.88, 0.90)	
4	406/ 1377 (29.5%)	15181/ 166503 (9.1%)	2.6 (2.4, 2.9)	99.4 (99.4, 99.4)	0.29 (27.08, 31.89)	90.9 (90.3, 91.4)	4.09 (3.67, 4.55)	0.98 (0.97, 0.99)	

Table S8. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of combined endpoint hospital mortality and/ or ventilation in the SARS-CoV-2 positive main cohort. Number of cases are provided together with absolute and relative frequencies (n, %) of died and/ or ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	20528/ 68594 (29.9%)	-	100 (100, 100)	0 (0, 0)	29.9 (29.6, 30.3)	-	1.00 (1.00, 1.00)	-	0.63 (0.62, 0.63)
≥ 1	8485/ 16655 (51.0%)	12043 /51939 (23.2%)	41.3 (40.7, 42.0)	83.0 (82.7, 83.3)	51.0 (50.2, 51.7)	76.8 (76.5, 77.2)	2.43 (2.37, 2.49)	0.71 (0.70, 0.71)	
≥ 2	1841/ 2404 (76.6%)	18687/ 66190 (28.2%)	9.0 (8.6, 9.4)	98.8 (98.7, 98.9)	76.6 (74.9, 78.3)	71.8 (71.4, 72.1)	7.66 (7.00, 8.37)	0.92 (0.92, 0.92)	
3	231/ 258 (89.5%)	20297/ 68336 (29.7%)	1.1 (1.0, 1.3)	99.9 (99.9, 100)	89.5 (85.8, 93.3)	70.3 (70.0, 70.6)	20.03 (13.45, 29.83)	0.99 (0.99, 0.99)	
qSOFA									
≥ 0	20528/ 68594 (29.9%)	-	100 (100, 100)	0 (0, 0)	29.9 (29.6, 30.3)	-	1.00 (1.00, 1.00)	-	0.64 (0.64, 0.65)
≥ 1	11696/ 26713 (43.8%)	8832/ 41881 (21.1%)	57.0 (56.3, 57.7)	68.8 (68.3, 69.2)	43.8 (43.2, 44.4)	78.9 (78.5, 79.3)	1.82 (1.79, 1.86)	0.63 (0.62, 0.63)	
≥ 2	2686/ 3918 (68.6%)	17842/ 64676 (27.6%)	13.1 (12.6, 13.5)	97.4 (97.3, 97.6)	68.6 (67.1, 70.0)	72.4 (72.1, 72.8)	5.10 (4.79, 5.44)	0.89 (0.89, 0.89)	
3	346/ 403 (85.9%)	20182/ 68191 (29.6%)	1.7 (1.5, 1.9)	99.9 (99.9, 99.9)	85.9 (82.5, 89.3)	70.4 (70.1, 70.7)	14.21 (10.75, 18.80)	0.98 (0.98, 0.99)	
CRB-65									
≥ 0	20528/ 68594 (29.9%)	-	100 (100, 100)	0 (0, 0)	29.9 (29.6, 30.3)	-	1.00 (1.00, 1.00)	-	0.71 (0.71, 0.71)
≥ 1	18153/ 46201 (39.3%)	2375/ 22393 (10.6%)	88.4 (88.0, 88.9)	41.6 (41.2, 42.1)	39.3 (38.8, 39.7)	89.4 (89.0, 89.8)	1.52 (1.50, 1.53)	0.28 (0.27, 0.29)	
≥ 2	7552/ 12993 (58.1%)	12976/ 55601 (23.3%)	36.8 (36.1, 37.4)	88.7 (88.4, 89.0)	58.1 (57.3, 59.0)	76.7 (76.3, 77.0)	3.25 (3.15, 3.35)	0.71 (0.71, 0.72)	
≥ 3	1679/ 2114 (79.4%)	18849/ 66480 (28.4%)	8.2 (7.8, 8.6)	99.1 (99.0, 99.2)	79.4 (77.5, 81.3)	71.7 (71.3, 72.0)	9.04 (8.16, 10.01)	0.93 (0.92, 0.93)	
4	222/ 247 (89.9%)	20306/ 68347 (29.7%)	1.1 (0.9, 1.2)	99.9 (99.9, 100)	89.9 (86.1, 93.6)	70.3 (70.0, 70.6)	20.79 (13.76, 31.43)	0.99(0.98, 0.99)	
qSOFA-65									
≥ 0	20528/ 68594 (29.9%)	-	100 (100, 100)	0 (0, 0)	29.9 (29.6, 30.3)	-	1.00 (1.00, 1.00)	-	0.72 (0.71, 0.72)
≥ 1	18954/ 50833 (37.3%)	1574/ 17761 (8.9%)	92.3 (92.0, 92.7)	33.7 (33.3, 34.1)	37.3 (36.9, 37.7)	91.1 (90.7, 91.6)	1.39 (1.38, 1.40)	0.23 (0.22, 0.24)	
≥ 2	10063/ 18720 (53.8%)	10465/ 49874 (21.0%)	49.0 (48.3, 49.7)	82.0 (81.6, 82.3)	53.8 (53.0, 54.5)	79.0 (78.7, 79.4)	2.72 (2.66, 2.79)	0.62 (0.61, 0.63)	
≥ 3	2435/ 3345 (72.8%)	18093/ 65249 (27.7%)	11.9 (11.4, 12.3)	98.1 (98.0, 98.2)	72.8 (71.0, 74.5)	72.3 (71.9, 72.6)	6.27 (5.83, 6.73)	0.90 (0.89, 0.90)	
4	325/ 374 (86.9%)	20203/ 68220 (29.6%)	1.6 (1.4, 1.8)	99.9 (99.9, 99.9)	86.9 (83.5, 90.3)	70.4 (70.1, 70.7)	15.53 (11.51, 20.96)	0.99 (0.98, 0.99)	

Table S9. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of combined endpoint hospital mortality and/ or ventilation in the SARS-CoV-2 negative main cohort. Number of cases are provided together with absolute and relative frequencies (n, %) of died and/ or ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	35158/ 167880 (20.9%)	-	100 (100, 100)	0 (0, 0)	20.9 (20.7, 21.1)	-	1.00 (1.00, 1.00)	-	0.63 (0.63, 0.64)
≥ 1	17568/ 51165 (34.3%)	17590/ 116715 (15.1%)	50.0 (49.9, 50.5)	74.7 (74.5, 74.9)	34.3 (33.9, 34.7)	84.9 (84.7, 85.1)	1.97 (1.95, 2.00)	0.67 (0.67, 0.67)	
≥ 2	4693/ 8251 (56.9%)	30465/ 159629 (19.1%)	13.3 (13.0, 13.7)	97.3 (97.2, 97.4)	56.9 (56.6, 57.2)	80.96 (80.5, 81.3)	4.98 (4.79, 5.18)	0.89 (0.89, 0.89)	
3	612/ 800 (76.5%)	34546/ 167080 (20.7%)	1.7 (1.6, 1.9)	99.9 (99.8, 99.9)	76.5 (76.3, 76.7)	79.3 (78.4, 80.2)	12.29 (11.37, 13.28)	0.98 (0.94, 1.03)	
qSOFA									
≥ 0	35158/ 167880 (20.9%)	-	100 (100, 100)	0 (0, 0)	20.9 (20.7, 21.1)	-	1.00 (1.00, 1.00)	-	0.65 (0.65, 0.66)
≥ 1	22111/ 70998 (31.1%)	13047/ 96882 (13.5%)	62.9 (62.4, 63.4)	63.2 (62.9, 63.4)	31.1 (30.8, 31.5)	86.5 (86.3, 86.7)	1.71 (1.69, 1.73)	0.59 (0.58, 0.59)	
≥ 2	7123/ 13515 (52.7%)	28035/ 154365 (18.2%)	20.3 (19.8, 20.7)	95.2 (95.1, 95.3)	52.7 (52.2, 53.2)	81.8 (81.5, 82.2)	4.21 (4.08, 4.33)	0.84 (0.83, 0.84)	
3	1159/ 1588 (73.0%)	33999/ 166292 (20.4%)	3.3 (3.1, 3.5)	99.7 (99.6, 99.7)	73.0 (72.7, 73.3)	79.6 (78.8, 80.3)	10.20 (9.66, 10.77)	0.97 (0.95, 1.00)	
CRB-65									
≥ 0	35158/ 167880 (20.9%)	-	100 (100, 100)	0 (0, 0)	20.9 (20.7, 21.1)	-	1.00 (1.00, 1.00)	-	0.65 (0.65, 0.66)
≥ 1	32454/ 137475 (23.6%)	2704/ 30405 (8.9%)	92.3 (92.0, 92.6)	20.9 (20.7, 21.1)	23.6 (23.4, 23.8)	91.1 (90.8, 91.4)	1.17 (1.16, 1.17)	0.37 (0.36, 0.37)	
≥ 2	15862/ 44199 (35.9%)	19296/ 123681 (15.6%)	45.1 (44.6, 45.6)	78.6 (78.4, 78.9)	35.9 (35.4, 36.3)	84.4 (84.2, 84.6)	2.11 (2.08, 2.14)	0.70 (0.69, 0.70)	
≥ 3	4164/ 7276 (57.2%)	30994/ 160604 (19.3%)	11.8 (11.5, 12.2)	97.7 (97.6, 97.7)	57.2 (56.7, 57.8)	80.7 (80.3, 81.1)	5.05 (4.84, 5.27)	0.90 (0.90, 0.91)	
4	528/ 699 (75.5%)	34630/ 167181 (20.7%)	1.5 (1.4, 1.6)	99.9 (99.9, 99.9)	75.5 (75.3, 75.8)	79.3 (78.3, 80.3)	11.66 (10.74, 12.65)	0.99 (0.95, 1.02)	
qSOFA-65									
≥ 0	35158/ 167880 (20.9%)	-	100 (100, 100)	0 (0, 0)	20.9 (20.7, 21.1)	-	1.00 (1.00, 1.00)	-	0.67 (0.67, 0.67)
≥ 1	33351/ 143437 (23.3%)	1807/ 24453 (7.4%)	94.9 (94.6, 95.1)	17.1 (16.9, 17.3)	23.3 (23.0, 23.5)	92.6 (92.3, 92.9)	1.14 (1.14, 1.15)	0.30 (0.30, 0.31)	
≥ 2	19871/ 59068 (33.6%)	15287/ 108812 (14.0%)	56.5 (56.0, 57.0)	70.5 (70.2, 70.7)	33.6 (33.3, 34.0)	86.0 (85.7, 86.2)	1.91 (1.89, 1.94)	0.62 (0.61, 0.62)	
≥ 3	6312/ 11652 (54.2%)	28846/ 156228 (18.5%)	18.0 (17.6, 18.4)	96.0 (95.9, 96.1)	54.2 (53.3, 55.1)	81.5 (81.2, 81.9)	4.46 (4.32, 4.61)	0.85 (0.85, 0.86)	
4	994/ 1377 (72.2%)	34164/ 166503 (20.5%)	2.8 (2.7, 3.0)	99.7 (99.7, 99.7)	0.72 (69.8, 74.6)	79.5 (78.7, 80.3)	9.80 (8.76, 10.96)	0.97 (0.97, 0.98)	

Table S10. Multivariable analyses for hospital mortality, need for mechanical ventilation and combined endpoints hospital mortality or/ and ventilation in the SARS-CoV-2 positive reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Risk ratio (RR) together with the 95% confidence interval (95% CI) and the corresponding p-value are provided. The results are based on Poisson regression modelling

	SARS-CoV-2 pos. mortality		SARS-CoV-2 pos. mechanical ventilation		SARS-CoV-2 pos. mortality and/ or mechanical ventilation	
	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Primary multivariable model						
CRB-65 Score						
confusion (C)	2.0 (1.83, 2.19)	0.00	1.74 (1.59, 1.90)	0.00	1.82 (1.69, 1.96)	0.00
respiratory rate at admission \geq 30 breaths/min (R)	1.73 (1.58, 1.89)	0.00	1.87 (1.74, 2.01)	0.00	1.75 (1.64, 1.87)	0.00
systolic blood pressure $<$ 90 or diastolic blood pressure \leq 60 mmHg (B)	1.49 (1.37, 1.62)	0.00	1.35 (1.26, 1.45)	0.00	1.34 (1.26, 1.43)	0.00
age \geq 65 years (65)	6.85 (6.24, 7.53)	0.00	1.27 (1.21, 1.33)	0.00	1.81 (1.73, 1.89)	0.00
qSOFA						
respiratory rate at admission \geq 22 breaths/min	1.71 (1.6, 1.83)	0.00	1.86 (1.76, 1.96)	0.00	1.71 (1.63, 1.79)	0.00
systolic blood pressure \leq 100 mmHg	1.47 (1.32, 1.65)	0.00	1.09 (0.98, 1.20)	0.12	1.25 (1.14, 1.36)	0.00

Table S11. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of hospital mortality in the SARS-CoV-2 positive reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Number of cases are provided together with absolute and relative frequencies (n, %) of died patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	4512/ 51015 (8.8%)	-	100 (100, 100)	0 (0, 0)	8.8 (8.0, 9.7)	-	1.00 (1.00, 1.00)	-	0.63 (0.62, 0.63)
≥ 1	1849/ 9649 (19.2%)	2663/ 41366 (6.4%)	41.0 (39.5, 42.4)	83.2 (82.9, 83.6)	19.2 (17.4, 21.0)	93.6 (93.3, 93.8)	2.44 (2.35, 2.54)	0.71 (0.70, 0.72)	
≥ 2	398/ 957 (41.6%)	4114/ 50058 (8.2%)	8.8 (8.0, 9.6)	98.8 (98.7, 98.9)	41.6 (36.8, 46.4)	91.8 (91.2, 92.4)	7.34 (6.52, 8.26)	0.92 (0.91, 0.93)	
3	54/ 74 (73.0%)	4458/ 50941 (8.8%)	1.2 (0.9, 1.5)	100 (99.9, 100)	73.0 (61.3, 84.7)	91.2 (89.4, 93.1)	27.83 (21.38, 36.22)	0.99 (0.87, 1.12)	
qSOFA									
≥ 0	4512/ 51015 (8.8%)	-	100 (100, 100)	0 (0, 0)	8.8 (8.2, 9.7)	-	1.00 (1.00, 1.00)	-	0.63 (0.63, 0.64)
≥ 1	2541/ 17372 (14.6%)	1971/ 33643 (5.9%)	56.3 (54.9, 57.8)	68.1 (67.7, 68.5)	14.6 (13.3, 16.0)	94.1 (93.9, 94.4)	1.77 (1.72, 1.82)	0.64 (0.63, 0.65)	
≥ 2	547/ 1672 (32.7%)	3965/ 49343 (8.0%)	12.1 (11.2, 13.1)	97.6 (97.4, 97.7)	32.7 (28.8, 36.6)	92.0 (91.5, 92.4)	5.01 (4.57, 5.50)	0.90 (0.89, 0.91)	
3	73/ 112 (65.2%)	4439/ 50903 (8.7%)	1.6 (1.2, 2.0)	99.9 (99.9, 99.9)	65.2 (54.4, 76.0)	91.3 (89.9, 92.7)	19.29 (15.49, 24.03)	0.98 (0.91, 1.06)	
CRB-65									
≥ 0	4512/ 51015 (8.8%)	-	100 (100, 100)	0 (0, 0)	8.8 (8.2, 9.7)	-	1.00 (1.00, 1.00)	-	0.75 (0.75, 0.76)
≥ 1	4195/ 2940 (14.3%)	317/ 21775 (1.5%)	93.0 (92.2, 93.7)	46.1 (45.7, 46.6)	14.3(13.3, 15.4)	98.5 (98.4, 98.7)	1.73 (1.71, 1.75)	0.15 (0.15, 0.16)	
≥ 2	1693/ 6267 (27.0%)	2819/ 44748 (6.3%)	37.5 (36.1, 38.9)	90.2 (89.9, 90.4)	27.0 (24.9, 29.1)	93.7(93.4, 94.0)	3.81 (3.65, 3.99)	0.69 (0.69, 0.70)	
≥ 3	356/ 716 (49.7%)	4156/ 50299 (8.3%)	7.9 (7.1, 8.7)	99.2 (99.1, 99.3)	49.7 (44.5, 54.9)	91.7 (91.0, 92.5)	10.19 (8.90, 11.67)	0.93 (0.92, 0.94)	
4	51/ 68 (75.0%)	4461/ 50947 (8.8%)	1.1 (0.8, 1.4)	100 (99.9, 100)	75.0 (63.3, 86.8)	91.2 (89.1, 93.4)	30.92 (23.80, 40.16)	0.99 (0.88, 1.12)	
qSOFA-65									
≥ 0	4512/ 51015 (8.8%)	-	100 (100, 100)	0 (0, 0)	8.8 (8.2, 9.7)	-	1.00 (1.00, 1.00)	-	0.75 (0.74, 0.76)
≥ 1	4312/ 33706 (12.8%)	200/ 17309 (1.2%)	95.6 (95.0, 96.2)	36.8 (36.4, 37.2)	12.8 (11.8, 13.8)	98.8 (98.7, 99.0)	1.51 (1.50, 1.53)	0.12 (0.12, 0.12)	
≥ 2	2292/ 9783 (23.4%)	2220/ 41232 (5.4%)	50.8 (49.3, 52.3)	83.9 (83.6, 84.2)	23.4 (21.7, 25.2)	94.6 (94.3, 94.9)	3.15 (3.05, 3.26)	0.59 (0.58, 0.59)	
≥ 3	485/ 1186 (40.9%)	4027/ 49829 (8.1%)	10.7 (9.8, 11.7)	98.5 (98.4, 98.6)	40.9 (36.5, 45.3)	91.9 (91.3, 92.5)	7.13 (6.41, 7.93)	0.91 (0.90, 0.92)	
4	66/ 92 (71.7%)	4446/ 50923 (8.7%)	1.5 (1.1, 1.8)	99.9 (99.9, 100)	71.7 (61.0, 82.5)	91.3 (89.6, 92.9)	26.16 (16.87, 40.57)	0.99 (0.97, 1.00)	

Table S12. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of mechanical ventilation in the SARS-CoV-2 positive reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Number of cases are provided together with absolute and relative frequencies (n, %) of ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	7119/ 51015(14.0%)	-	100 (100, 100)	0 (0, 0)	14.0 (13.7, 14.3)	-	1.00 (1.00, 1.00)	-	0.60 (0.59, 0.60)
≥ 1	2504/ 9649 (26.0%)	4615/ 41366 (11.2%)	35.2 (34.1, 36.3)	83.7 (83.4, 84.1)	26.0 (25.1, 26.8)	88.8 (88.5, 89.1)	2.16 (2.08, 2.24)	0.77 (0.77, 0.78)	
≥ 2	443/ 957 (46.3%)	6676/ 50058 (13.3%)	6.2 (5.7, 6.8)	98.8 (98.7, 98.9)	46.3 (45.7, 46.8)	86.7 (85.9, 87.4)	5.31 (4.72, 5.98)	0.95 (0.94, 0.96)	
3	43/ 74 (58.1%)	7076/ 50941 (13.9%)	0.6 (0.4, 0.8)	99.9 (99.9, 100)	58.1 (57.6, 58.6)	86.1 (83.8, 88.4)	8.55 (6.35, 11.51)	0.99 (0.88, 1.13)	
qSOFA									
≥ 0	7119/ 51015 (14.0%)	-	100 (100, 100)	0 (0, 0)	14.0 (13.7, 14.3)	-	1.00 (1.00, 1.00)	-	0.63 (0.62, 0.63)
≥ 1	3887/ 17372 (22.4%)	3232/ 33643 (9.6%)	54.6 (53.4, 55.8)	69.3 (68.8, 69.7)	22.4 (21.8, 23.0)	90.4 (90.1, 90.7)	1.78 (1.73, 1.82)	0.66 (0.65, 0.66)	
≥ 2	607/ 1672 (36.3%)	6512/ 49343 (13.2%)	8.5 (7.9, 9.2)	97.6 (97.4, 97.7)	36.3 (35.7, 36.9)	86.8 (86.3, 87.3)	3.51 (3.20, 3.86)	0.94 (0.93, 0.94)	
3	54/ 112 (48.2%)	7065/ 50903 (13.9%)	0.8 (0.6, 1.0)	99.9 (99.8, 99.9)	48.2 (47.7, 48.7)	86.1 (84.4, 87.8)	5.74 (4.41, 7.48)	0.99 (0.91, 1.09)	
CRB-65									
≥ 0	7119/ 51015 (14.0%)	-	100 (100, 100)	0 (0, 0)	14.0 (13.7, 14.3)	-	1.00 (1.00, 1.00)	-	0.61 (0.60, 0.62)
≥ 1	5026/ 29240 (17.2%)	2093/ 21775 (9.6%)	70.6 (69.5, 71.7)	44.8 (44.4, 45.3)	17.2 (16.8, 17.6)	90.4 (90.0, 90.8)	1.28 (1.26, 1.30)	0.66 (0.64, 0.67)	
≥ 2	1750/ 6267 (27.9%)	5369/ 44748 (12.0%)	24.6 (23.6, 25.6)	89.7 (89.4, 90.0)	27.9 (26.8, 29.0)	88.0 (87.6, 88.4)	2.39 (2.28, 2.50)	0.84 (0.83, 0.85)	
≥ 3	318/ 716 (44.4%)	6801/ 50299 (13.5%)	4.5 (4.0, 4.9)	99.1 (99.0, 99.2)	44.4 (43.7, 45.2)	86.5 (85.6, 87.4)	4.93 (4.30, 5.65)	0.96 (0.95, 0.98)	
4	38/ 68 (55.9%)	7081/ 50947 (13.9%)	0.5 (0.4, 0.7)	99.9 (99.9, 100)	55.9 (55.4, 56.4)	86.1 (86.4, 88.8)	7.81 (5.70, 10.70)	1.00 (0.86, 1.15)	
qSOFA-65									
≥ 0	7119/ 51015 (14.0%)	-	100 (100, 100)	0 (0, 0)	14.0 (13.7, 14.3)	-	1.00 (1.00, 1.00)	-	0.63 (0.62, 0.64)
≥ 1	5734/ 33706 (17.0%)	1385/ 17309 (8.0%)	80.5 (79.6, 81.5)	36.3 (35.8, 36.7)	17.0 (16.6, 17.4)	92.0 (91.6, 92.4)	1.26 (1.25, 1.28)	0.54 (0.53, 0.55)	
≥ 2	2492/ 9783 (25.5%)	4627/ 41232 (11.2%)	35.0 (33.9, 36.1)	83.4 (83.0, 83.7)	25.5 (24.6, 26.3)	88.8 (88.4, 89.2)	2.11 (2.03, 2.18)	0.78 (0.77, 0.79)	
≥ 3	424/ 1186 (35.8%)	6695/ 49829 (13.4%)	6.0 (5.4, 6.5)	98.3 (98.1, 98.4)	35.8 (33.0, 38.5)	86.6 (85.8, 87.3)	3.43 (3.07, 3.83)	0.96 (0.95, 0.97)	
4	40/ 92 (43.4%)	7079/ 50923 (13.9%)	0.6 (0.4, 0.7)	99.9 (99.8, 99.9)	43.5 (33.3, 53.6)	86.1 (84.0, 88.1)	4.74 (3.20, 7.04)	1.00 (0.98, 1.01)	

Table S13. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of combined endpoint hospital mortality and/ or mechanical ventilation in the SARS-CoV-2 positive reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Number of cases are provided together with absolute and relative frequencies (n, %) of died and/ or ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	9135/ 51015 (17.9%)	-	100 (100, 100)	0 (0, 0)	17.9 (17.6, 18.2)	-	1.00 (1.00, 1.00)	-	0.60 (0.60, 0.61)
≥ 1	3242/ 9649 (33.6%)	5893/ 41366 (14.2%)	35.5 (34.5, 36.5)	84.7 (84.4, 85.0)	33.6 (32.7, 34.5)	85.8 (85.4, 86.1)	2.32 (2.24, 2.40)	0.76 (0.76, 0.77)	
≥ 2	589/ 957 (61.5%)	8546/ 50058 (17.1%)	6.4 (5.9, 7.0)	99.1 (99.0, 99.2)	61.5 (58.5, 64.6)	82.9 (82.6, 83.3)	7.34 (6.49, 8.30)	0.94 (0.94, 0.95)	
3	61/ 74 (82.4%)	9074/ 50941 (17.8%)	0.7 (0.5, 0.8)	100 (100, 100)	82.4 (73.8, 91.1)	82.2 (81.9, 82.5)	21.51 (11.83, 39.13)	0.99 (0.99, 1.00)	
qSOFA									
≥ 0	9135/ 51015 (17.9%)	-	100 (100, 100)	0 (0, 0)	17.9 (17.6, 18.2)	-	1.00 (1.00, 1.00)	-	0.63 (0.62, 0.63)
≥ 1	4892/ 17372 (28.2%)	4243/ 33643 (12.6%)	53.6 (52.5, 54.6)	70.2 (69.8, 70.6)	28.2 (27.5, 28.8)	87.4 (87.0, 87.7)	1.80 (1.75, 1.84)	0.66 (0.66, 0.67)	
≥ 2	822/ 1672 (49.2%)	8313/ 49343 (16.8%)	9.0 (8.4, 9.6)	98.0 (97.8, 98.1)	49.2 (46.8, 51.6)	83.2 (82.8, 83.5)	4.43 (4.05, 4.85)	0.93 (0.93, 0.93)	
3	85/ 112 (75.9%)	9050/ 50903 (17.8%)	0.9 (0.7, 1.1)	99.9 (99.9, 100)	75.9 (68.0, 83.8)	82.2 (81.9, 82.6)	14.43 (9.37, 22.24)	0.99 (0.99, 0.99)	
CRB-65									
≥ 0	9135/ 51015 (17.9%)	-	100 (100, 100)	0 (0, 0)	17.9 (17.6, 18.2)	-	1.00 (1.00, 1.00)	-	0.66 (0.65, 0.66)
≥ 1	6996/ 26240 (23.9%)	2139/ 21775 (9.8%)	76.6 (75.5, 77.5)	46.9 (46.4, 47.4)	23.9 (23.4, 24.4)	90.2 (89.8, 90.6)	1.44 (1.42, 1.46)	0.50 (0.48, 0.52)	
≥ 2	2465/ 6267 (39.9%)	6670/ 44748 (14.9%)	27.0 (26.1, 27.9)	90.9 (90.6, 91.2)	39.3 (38.1, 40.5)	85.1 (84.8, 85.4)	2.97 (2.84, 3.11)	0.80 (0.79, 0.81)	
≥ 3	461/ 716 (64.4%)	8674/ 50299 (17.2%)	5.0 (4.6, 5.5)	99.4 (99.3, 99.5)	64.4 (60.1, 68.7)	82.6 (82.4, 83.1)	8.29 (7.16, 9.60)	0.96 (0.95, 0.96)	
4	56/ 68 (82.4%)	9079/ 50947 (17.8%)	0.61 (0.5, 0.8)	100 (100, 100)	82.4 (73.3, 91.4)	82.2 (81.8, 82.5)	21.39 (11.47, 39.89)	0.99 (0.99, 1.00)	
qSOFA-65									
≥ 0	9135/ 51015 (17.9%)	-	100 (100, 100)	0 (0, 0)	17.9 (17.6, 18.2)	-	1.00 (1.00, 1.00)	-	0.67 (0.66, 0.67)
≥ 1	7714/ 33706 (22.9%)	1421/ 17309 (8.2%)	84.4 (83.7, 85.2)	37.9 (37.5, 38.4)	22.9 (22.4, 23.3)	91.8 (91.4, 92.2)	1.36 (1.34, 1.38)	0.41 (0.39, 0.43)	
≥ 2	3467/ 9783 (35.4%)	5668/ 41323 (13.7%)	38.0 (37.0, 38.2)	84.9 (84.6, 85.3)	35.4 (34.5, 36.4)	86.3 (85.9, 86.6)	2.51 (2.43, 2.61)	0.73 (0.72, 0.74)	
≥ 3	634/ 1186 (53.5%)	8501/ 49829 (17.1%)	6.9 (6.4, 7.5)	98.7 (98.6, 98.8)	53.5 (49.6, 57.3)	82.9 (82.6, 83.3)	5.27 (4.73, 5.86)	0.94 (0.94, 0.95)	
4	70/ 92 (76.1%)	9065/ 50923 (17.8%)	0.8 (0.6, 0.9)	99.9 (99.9, 100)	76.1 (67.4, 84.8)	82.2 (81.9, 82.5)	14.59 (9.04, 23.54)	0.99 (0.99, 0.99)	

Table S14. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of hospital mortality in the SARS-CoV-2 negative reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Number of cases are provided together with absolute and relative frequencies (n, %) of died patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	6766/ 111037 (6.1%)	-	100 (100, 100)	0 (0, 0)	6.1 (6.0, 6.2)	-	1.00 (1.00, 1.00)	-	0.63 (0.63, 0.64)
≥ 1	3216/ 27050 (11.9%)	3550/ 83987 (4.2%)	47.5 (46.3, 48.7)	77.1 (76.9, 77.4)	11.9 (11.5, 12.3)	95.8 (95.6, 95.9)	2.08 (2.02, 2.14)	0.68 (0.67, 0.69)	
≥ 2	821/ 3285 (25.0%)	5945/ 107752 (5.5%)	12.1 (11.4, 12.9)	97.6 (97.5, 97.7)	25.0 (24.7, 25.3)	94.5 (94.2, 94.8)	5.13 (4.79, 5.51)	0.90 (0.89, 0.90)	
3	121/ 274 (44.2%)	6645/ 110763 (6.0%)	1.8 (1.5, 2.1)	99.9 (99.8, 99.9)	44.2 (43.9, 44.5)	94.0 (93.2, 94.8)	12.19 (10.23, 14.52)	0.98 (0.92, 1.06)	
qSOFA									
≥ 0	6766/ 111037 (6.1%)	-	100 (100, 100)	0 (0, 0)	6.1 (6.0, 6.2)	-	1.00 (1.00, 1.00)	-	0.64 (0.64, 0.65)
≥ 1	4032/ 40580 (9.9%)	2734/ 70457 (3.9%)	59.6 (58.4, 60.8)	64.9 (64.7, 65.2)	9.9 (9.6, 10.2)	96.1 (96.0, 96.3)	1.70 (1.66, 1.74)	0.62 (0.61, 0.63)	
≥ 2	1229/ 5566 (22.1%)	5537/ 105471 (5.2%)	18.2 (17.2, 19.1)	95.8 (95.7, 96.0)	22.1 (21.6, 22.5)	94.8 (94.5, 95.0)	4.37 (4.14, 4.61)	0.85 (0.85, 0.86)	
3	228/ 536 (42.5%)	6538/ 110501 (5.9%)	3.4 (2.9, 3.8)	99.7 (99.7, 99.7)	42.5 (42.2, 42.9)	94.1 (93.4, 94.7)	11.41 (10.11, 12.87)	0.97 (0.93, 1.00)	
CRB-65									
≥ 0	6766/ 111037 (6.1%)	-	100 (100, 100)	0 (0, 0)	6.1 (6.0, 6.2)	-	1.00 (1.00, 1.00)	-	0.68 (0.67, 0.68)
≥ 1	6352/ 84366 (7.5%)	414/ 26787 (1.5%)	93.9 (93.3, 94.5)	25.2 (24.9, 25.4)	7.5 (7.4, 7.7)	98.4 (98.3, 98.6)	1.25 (1.25, 1.26)	0.24 (0.23, 0.25)	
≥ 2	2926/ 21978 (13.3%)	3840/ 89175 (4.3%)	43.2 (42.1, 44.4)	81.7 (81.5, 82.0)	13.3 (12.9, 13.8)	95.7 (95.5, 95.8)	2.37 (2.30, 2.44)	0.69 (0.69, 0.70)	
≥ 3	698/ 2689 (26.0%)	6068/ 108464 (5.6%)	10.3 (9.6, 11.0)	98.1 (98.0, 98.2)	26.0 (25.4, 26.5)	94.4 (94.1, 94.7)	5.40 (5.00, 5.83)	0.91 (0.91, 0.92)	
4	101/ 217 (46.5%)	6665/ 110936 (6.0%)	1.5 (1.2, 1.8)	99.9 (99.9, 99.9)	46.5 (46.2, 46.9)	94.0 (93.0, 94.9)	13.42 (11.16, 16.14)	0.99 (0.93, 1.05)	
qSOFA-65									
≥ 0	6766/ 111037 (6.1%)	-	100 (100, 100)	0 (0, 0)	6.1 (6.0, 6.2)	-	1.00 (1.00, 1.00)	-	0.68 (0.68, 0.69)
≥ 1	6498/ 89351 (7.3%)	268/ 21686 (1.2%)	96.0 (95.6, 96.5)	20.5 (20.3, 20.8)	7.3 (7.1, 7.4)	98.8 (98.6, 98.9)	1.21 (1.20, 1.21)	0.19 (0.19, 0.20)	
≥ 2	3649/ 31137 (11.7%)	3117/ 79900 (3.9%)	53.9 (52.7, 55.1)	73.6 (73.4, 73.9)	11.7 (11.4, 12.1)	96.1 (95.9, 96.3)	2.05 (2.00, 2.09)	0.63 (0.62, 0.63)	
≥ 3	1073/ 4414 (24.3%)	5693/ 106623 (5.3%)	15.9 (15.0, 16.7)	96.8 (96.7, 96.9)	24.3 (23.0, 25.6)	94.7 (94.4, 94.9)	4.95 (4.66, 5.25)	0.87 (0.86, 0.88)	
4	188/ 421 (44.7%)	6578/ 110616 (5.9%)	2.8 (2.4, 3.2)	99.8 (99.7, 99.8)	44.7 (39.9, 49.4)	94.1 (93.3, 94.8)	12.43 (10.39, 14.88)	0.97 (0.97, 0.98)	

Table S15. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of mechanical ventilation in the SARS-CoV-2 negative reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Number of cases are provided together with absolute and relative frequencies (n, %) of ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	9214/ 111037 (8.3%)	-	100 (100, 100)	0 (0, 0)	8.3 (8.1, 8.5)	-	1.00 (1.00, 1.00)	-	0.62 (0.62, 0.63)
≥ 1	4158/ 27050 (15.4%)	5056/ 83987 (6.0%)	45.1 (44.1, 46.1)	77.5 (77.3, 77.8)	15.4 (14.9, 15.8)	94.0 (93.8, 94.1)	2.01 (1.96, 2.06)	0.71 (0.70, 0.71)	
≥ 2	1104/ 3285 (33.6%)	8110/ 107752 (7.5%)	12.0 (11.3, 12.6)	97.9 (97.8, 97.9)	33.6 (33.3, 34.0)	92.5 (92.1, 92.8)	5.59 (5.24, 5.97)	0.90 (0.89, 0.91)	
3	140/ 274 (51.1%)	9074/ 110763 (8.2%)	1.5 (1.3, 1.8)	99.9 (99.8, 99.9)	51.1 (50.8, 51.4)	91.8 (90.8, 92.8)	11.55 (9.81, 13.59)	0.99 (0.92, 1.05)	
qSOFA									
≥ 0	9214/ 111037 (8.3%)	-	100 (100, 100)	0 (0, 0)	8.3 (8.1, 8.5)	-	1.00 (1.00, 1.00)	-	0.65 (0.65, 0.66)
≥ 1	5631/ 40580 (13.9%)	3583/ 70457 (5.1%)	61.1 (60.1, 62.1)	65.7 (65.4, 66.0)	13.9 (13.5, 14.2)	94.9 (94.8, 95.1)	1.78 (1.75, 1.81)	0.59 (0.59, 0.60)	
≥ 2	1550/ 5566 (27.8%)	7664/ 105471 (7.3%)	16.8 (16.1, 17.6)	96.1 (95.9, 96.2)	27.8 (27.3, 28.3)	92.7 (92.5, 93.0)	4.27 (4.05, 4.49)	0.87 (0.86, 0.87)	
3	255/ 536 (47.6%)	8959/ 110501 (8.1%)	2.8 (2.4, 3.1)	99.7 (99.7, 99.8)	47.6 (47.2, 47.9)	91.9 (91.1, 92.6)	10.03 (8.91, 11.28)	0.98 (0.93, 1.02)	
CRB-65									
≥ 0	9214/ 111037 (8.3%)	-	100 (100, 100)	0 (0, 0)	8.3 (8.1, 8.5)	-	1.00 (1.00, 1.00)	-	0.60 (0.60, 0.60)
≥ 1	7613/ 84366 (9.0%)	1601/ 26671 (6.0%)	82.6 (81.9, 83.4)	24.6 (24.4, 24.9)	9.0 (8.8, 9.2)	94.0 (93.7, 94.3)	1.10 (1.09, 1.11)	0.71 (0.69, 0.72)	
≥ 2	3261/ 21978 (14.8%)	5953/ 89059 (6.7%)	35.4 (34.4, 36.4)	81.6 (81.4, 81.9)	14.8 (14.4, 15.3)	93.3 (93.1, 93.5)	1.93 (1.87, 1.98)	0.79 (0.78, 0.80)	
≥ 3	812/ 2689 (30.2%)	8402/ 108348 (7.8%)	8.8 (8.2, 9.4)	98.2 (98.1, 98.2)	30.2 (29.6, 30.8)	92.2 (91.9, 92.6)	4.78 (4.44, 5.15)	0.93 (0.92, 0.94)	
4	96/ 217 (44.2%)	9118/ 110820 (8.2%)	1.0 (0.8, 1.2)	99.9 (99.9, 99.9)	44.2 (43.9, 44.6)	91.8 (90.7, 92.9)	8.77 (7.22, 10.65)	0.99 (0.93, 1.1)	
qSOFA-65									
≥ 0	9214/ 111037 (8.3%)	-	100 (100, 100)	0 (0, 0)	8.3 (8.1, 8.5)	-	1.00 (1.00, 1.00)	-	0.62 (0.62, 0.63)
≥ 1	8169/ 89351 (9.1%)	1045/ 21686 (4.8%)	88.7 (88.0, 89.3)	20.3 (20.0, 20.5)	9.1 (9.0, 9.3)	95.2 (94.9, 95.5)	1.11 (1.10, 1.12)	0.56 (0.55, 0.57)	
≥ 2	4331/ 31137 (13.9%)	4883/ 79900 (6.1%)	47.0 (46.0, 48.0)	73.7 (73.4, 73.9)	13.9 (13.5, 14.3)	93.9 (93.7, 94.1)	1.79 (1.75, 1.83)	0.72 (0.71, 0.73)	
≥ 3	1144/ 4414 (25.9%)	8070/ 106623 (7.6%)	12.4 (11.7, 13.1)	96.8 (96.7, 96.9)	25.9 (24.6, 27.2)	92.4 (92.1, 92.7)	3.87 (3.64, 4.10)	0.90 (0.90, 0.91)	
4	172/ 421 (40.9%)	9042/ 110616 (8.2%)	1.9 (1.6, 2.1)	99.8 (99.7, 99.8)	40.9 (36.2, 45.6)	91.8 (91.0, 92.7)	7.63 (6.36, 9.16)	0.98 (0.97, 0.99)	

Table S16. Performance measures of CRB, CRB-65, qSOFA and qSOFA-65 in terms of combined endpoint hospital mortality and/ or mechanical ventilation in the SARS-CoV-2 negative reduced cohort 1 (after excluding patients with chronically bedridden, admission from nursing home and palliative treatment goal). Number of cases are provided together with absolute and relative frequencies (n, %) of died and/ or ventilated patients.

Score cut-off	Outcome present (n/N, %) with score values		Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]	Positive LR	Negative LR	AUC
	Larger than or equal to the cut-off	Smaller than the cut-off							
CRB									
≥ 0	13339/ 111037 (12.0%)	-	100 (100, 100)	0 (0, 0)	12.0 (11.8, 12.2)	-	1.00 (1.00, 1.00)	-	0.62 (0.62, 0.63)
≥ 1	5929/ 27050 (21.9%)	7410/ 83987 (8.8%)	44.4 (43.6, 45.3)	78.4 (78.1, 78.6)	21.9 (21.4, 22.4)	91.2 (91.0, 91.4)	2.06 (2.01, 2.10)	0.71 (0.70, 0.71)	
≥ 2	1456/ 3285 (44.3%)	11883/ 107752 (11.0%)	10.9 (10.4, 11.4)	98.1 (98.0, 98.2)	44.3 (44.0, 44.7)	89.0 (88.6, 89.4)	5.83 (5.48, 6.21)	0.91 (0.90, 0.91)	
3	190/ 274 (69.3%)	13149/ 110763 (11.9%)	1.4 (1.2, 1.6)	99.9 (99.9, 99.9)	69.3 (69.0, 69.6)	88.1 (87.0, 89.3)	16.57 (14.40, 19.06)	0.99 (0.92, 1.05)	
qSOFA									
≥ 0	13339/ 111037 (12.0%)	-	100 (100, 100)	0 (0, 0)	12.0 (11.8, 12.2)	-	1.00 (1.00, 1.00)	-	0.64 (0.64, 0.65)
≥ 1	7870/ 40580 (19.4%)	5469/ 70457 (7.8%)	59.0 (58.2, 59.8)	66.5 (66.2, 66.8)	19.4 (19.0, 19.8)	92.2 (92.0, 92.4)	1.76 (1.73, 1.79)	0.62 (0.61, 0.62)	
≥ 2	2165/ 5566 (38.9%)	11174/ 105471 (10.6%)	16.2 (15.6, 16.9)	96.5 (96.4, 96.6)	38.9 (38.3, 39.4)	89.4 (89.1, 89.7)	4.66 (4.44, 4.89)	0.87 (0.86, 0.87)	
3	354/ 536 (66.0%)	12985/ 110501 (11.8%)	2.7 (2.4, 2.9)	99.8 (99.8, 99.8)	66.0 (65.7, 66.4)	88.2 (87.4, 89.1)	14.25 (12.90, 15.74)	0.98 (0.93, 1.02)	
CRB-65									
≥ 0	13339/ 111037 (12.0%)	-	100 (100, 100)	0 (0, 0)	12.0 (11.8, 12.2)	-	1.00 (1.00, 1.00)	-	0.63 (0.62, 0.63)
≥ 1	11578/ 84366 (13.7%)	1761/ 26671 (6.6%)	86.8 (86.2, 87.4)	25.5 (25.2, 25.8)	13.7 (13.5, 14.0)	93.4 (93.1, 93.7)	1.17 (1.16, 1.17)	0.52 (0.51, 0.53)	
≥ 2	4949/ 21978 (22.5%)	8390/ 89059 (9.4%)	37.1 (36.3, 37.9)	82.6 (82.3, 82.8)	22.5 (22.0, 23.1)	90.6 (90.4, 90.8)	2.13 (2.08, 2.18)	0.76 (0.76, 0.77)	
≥ 3	1147/ 2689 (42.7%)	12192/ 108348 (11.3%)	8.8 (8.1, 9.1)	98.4 (98.3, 98.5)	42.7 (42.0, 43.3)	88.7 (88.3, 89.2)	5.45 (5.08, 5.84)	0.93 (0.92, 0.93)	
4	143/ 217 (65.9%)	13196/ 110820 (11.9%)	1.1 (0.9, 1.2)	99.9 (99.9, 99.9)	65.9 (65.6, 66.2)	88.1 (86.8, 89.4)	14.15 (12.08, 16.59)	0.99 (0.93, 1.06)	
qSOFA-65									
≥ 0	13339/ 111037 (12.0%)	-	100 (100, 100)	0 (0, 0)	12.0 (11.8, 12.2)	-	1.00 (1.00, 1.00)	-	0.65 (0.64, 0.65)
≥ 1	12177/ 89351 (13.6%)	1162/ 21686 (5.4%)	91.3 (90.8, 91.8)	21.0 (20.8, 21.3)	13.6 (13.4, 13.9)	94.6 (94.3, 94.9)	1.16 (1.15, 1.16)	0.41 (0.41, 0.42)	
≥ 2	6465/ 31137 (20.8%)	6874/ 79900 (8.6%)	48.5 (47.6, 49.3)	74.7 (74.5, 75.0)	20.8 (20.3, 21.2)	91.4 (91.2, 91.6)	1.92 (1.88, 1.96)	0.69 (0.68, 0.70)	
≥ 3	1726/ 4414 (39.1%)	11613/ 106623 (10.9%)	12.9 (12.4, 13.5)	97.2 (97.1, 97.4)	39.1 (37.7, 40.5)	89.1 (88.7, 89.5)	4.70 (4.46, 4.96)	0.90 (0.89, 0.90)	
4	263/ 421 (62.5%)	13076/ 110616 (11.8%)	2.0 (1.7, 2.2)	99.8 (99.8, 99.9)	62.5 (57.8, 67.1)	88.2 (87.2, 89.2)	12.19 (10.10, 14.71)	0.98 (0.97, 0.99)	