Derivation and validation of a risk-stratification model for probable or proven COVID-19 patients in Emergency Departments: the revised HOME-CoV score.

Running headline: Prognostic scores for COVID-19.

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Key Message

What is already known on this subject

- For emergency departments, early identification of COVID-19 patients who can be safely managed at home has been a major challenge to maintain patient care capacity.
- The HOME-CoV uses solely clinical data to determine which potentially positive COVID-19 patients are unlikely to have adverse events, and has been validated in a prospective study of 3000 patients with an AUC of 0.81.

What this study adds

- To improve its discriminatory power, we derived a Revised HOME-CoV score using 7 clinical variables and validated it on a different population.
- The optimised, uniquely clinical score had an AUC of 85.8 (95% CI 80.6 to 91.0) and negative predictive value of 99% and would allow 73% of patients to be discharged home.
- The Revised HOME-CoV score has the highest AUC compared with other common scores, although the difference is not statistically significant.

How this study might affect research, practice or policy

- The Revised HOME-CoV score based on 7 clinical items could be used in emergency departments to identify patients likely to have Covid-19 that do not require hospital admission.

ABSTRACT

Background

The HOME-CoV score is a validated list of uniquely clinical criteria indicating which patients with probable or proven COVID-19 can be treated at home. The aims of this study were to optimize the score to improve its ability to discriminate between patients who do and don't need admission.

Methods

A Revised HOME-CoV score was derived using data from a previous prospective multicenter study which evaluated the original Home-CoV score. Patients with proven or probable COVID-19 attending 34 EDs in France, Monaco and Belgium between April to May 2020 were included. The population was split into a derivation and validation sample corresponding to the observational and interventional phases of the original study. The main outcome was non-invasive or invasive ventilation or all-cause death within 7 days following inclusion. Two threshold values were defined using a sensitivity of > 0.9 and a specificity of > 0.9 to identify low-risk and high-risk patients, respectively. The Revised HOME-CoV score was then validated by retrospectively applying it to patients in the same EDs with proven or probable COVID-19 during the interventional phase. The revised HOME-CoV score was also tested against original HOME-CoV, qCSI, qSOFA, CRB65 and SMART-COP in this validation cohort.

Results

There were 1696 patients in the derivation cohort of whom 65 (3.8%) required non-invasive ventilation or mechanical ventilation or died within 7 days and 1304 patients in the validation cohort of whom 22 (1.7%) had a progression of illness. The revised score included seven clinical criteria. The AUC was 87.6 (95% CI 84.7 to 90.6). The cutoffs to define low-risk and high-risk patients were <2 and >3, respectively. In the validation cohort, the AUC was 85.8 (95% CI 80.6 to 91.0). A score of < 2 qualified 73% of patients as low risk with a sensitivity of 0.77 (0.55-0.92) and a negative predictive value of 0.99 (0.99-1.00).

Conclusion

The revised HOME-CoV score, which does not require laboratory testing, may allow accurate risk stratification and safely qualify a significant proportion of patients with probable or proven COVID-19 for home treatment.

Key Words: COVID-19; risk stratification, prognostic tool; score validation; score-based decision-making

BACKGROUND

The clinical spectrum of COVID-19 is broad, ranging from simple rhinitis to major pulmonary disease and death [1,2]. 80% of COVID-19 patients have mild or moderate infection but approximately 2% to 4% of overall patients will require mechanical ventilation for Acute Respiratory Distress Syndrome (ARDS)[3,4]. For some patients, the deterioration is rapid after an initial period of relatively mild symptoms, making the decision to discharge patients home challenging. However, particularly during surges, there is a need to rationalize hospital care to admit those at the highest risk of adverse outcomes. A reliable risk assessment model is therefore required to standardize practice and guide frontline physicians in the decision to hospitalize or manage patients with mild or intermediate COVID-19 at home.

Several clinical and biological features have been identified as independent mortality risk factors in COVID-19 [5–7]. Risk assessment models and triaging tools have been proposed, especially for referring COVID-19 patients to intensive care units.[8–10] However, a living systematic review of COVID-19 prediction models conducted in collaboration with the Cochrane Prognosis Methods Group, found that all prognostic scores have too high a risk of bias to recommend their use in routine practice and several require the results of laboratory testing [11]. The authors of the review offer methodological guidance to avoid the use of unreliable and possibly harmful models in guiding clinical decision-making, and recommend, i) building prediction models based on previous literature and expert consensus rather than selecting predictors in a purely data driven way, ii) developing and validating the model on a dataset of the target population in which it serves a clinical need, and iii) focusing on validating and updating promising currently available models.

In a previous study using a Delphi method, we developed the "**H**ospitalization or **O**utpatient **M**anag**E**ment of patients with SARS-**CoV**-2 infection" (HOME-CoV) score which relies only on clinical observations, with no laboratory data needed. [12]. The performance of the HOME-CoV score in defining a subgroup of patients with proven or probable COVID-19 who can be safely managed at home were recently confirmed in a prospective implementation before and after study: the HOME-CoV trial (NCT04338841,[13]). This score initially had two levels and did not include age as a factor. The AUC of the original HOME-CoV score was 80.9 (95% CI 76.3 to 85.6).

The main aim of the present study was to optimize the HOME-CoV score to a score that would be easy to apply and interpret and have 3 risk levels: low-risk patients who could be safely managed at home, intermediate-risk patients who may require hospitalization and high-risk patients who may benefit from intensive care. We hence set out to derive and internally validate an updated version: the revised HOME-CoV score.

METHODS

Study design

We undertook a retrospective analysis of a prospective database, using data from a multicenter before and after implementation trial aimed at validating the original HOME-CoV score [13]. The original HOME-CoV score contained 8 clinical criteria easily assessable at ED presentation (Table 1).

The first step was derivation of a revised HOME-CoV score to enhance the predictive performance of the original HOME-CoV score through the inclusion of clinical predictors identified in other models and the exclusion of variables with low information value. The second step was validation of the revised HOME-CoV score in an

independent cohort consisting of the patients from the original interventional study. The third step was comparison of the performance of the revised and the original HOME-CoV score to those of other assessment models proposed for risk stratification of COVID-19 patients: qCSI, qSOFA, CURB65, CRB65 and SMART-COP in the validation cohort [10,14–16] (Table 1). We adhered to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) checklist (Appendix 1).

Source of data

We used data from two distinct and independent phases of a prospective quasi-experimental before and after prospective multicenter trial, performed in 34 EDs in France (31), the Principality of Monaco (1) and Belgium (2) from April 9 to May 11, 2020 (n=3000 patients) (Table S1). Patients were eligible for inclusion if they provided informed consent, were at least 18 years old, had symptomatic COVID-19 confirmed by a positive SARS-CoV-2 Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR), or where the treating emergency physician thought that COVID-19 was the most likely diagnosis for the presenting symptoms. Only mild and moderate cases of COVID-19 were included (defined subjectively by the physician). Patients were excluded if the main diagnostic impression in the ED was not a SARS-CoV-2 infection, if they required care in an ICU or a resuscitation unit, if a decision to limit active therapies was made, or if follow-up at 28 days was not possible. Patient characteristics and clinical data were collected prospectively at ED presentation. Patients were followed-up at Day 7 and Day 28 by phone and their clinical status was recorded according to the Ordinal Scale for Clinical Improvement for COVID-19 patients from the World Health

Organization (WHO-OSCI) (Figure S1) [17]. The date of each change in WHO-OSCI status was also recorded to allow analysis over time.

Outcome

The main outcome was progression of illness within 7 days after ED presentation, defined according to the World Health Organization as a hospitalized patient with severe disease, under non-invasive ventilation or high-flow nasal oxygen therapy (stage 5), requiring intubation and invasive ventilation (stage 6), and/or additional organ support (stage 7) or who died, whatever the cause (stage 8) (Figure S1) [17].

Revised HOME-CoV Score

To develop the revised HOME-CoV score, we assessed whether inclusion of clinical variables included in other risk stratification models used for Covid-19. would improve the performance of the original HOME-CoV score, and conversely, if the exclusion of clinical variables from the original score would worsen the performance of the original HOME-CoV score (Table 1). To facilitate the implementation of the revised HOME-CoV score in the practice of emergency and primary care physicians, we did not include biochemical variables.

In the derivation cohort (observational period), a logistic regression model was developed to assess the discriminant value of each criterion of the original score and of age over 65 years for progression of illness (WHO-OSCI ≥5). In order to select the easiest to use model with the highest predictive value, a selection of variables allowing the optimization of the Akaïke Information Criterion (AIC) was carried out in a manual backward selection process[18]. All significant variables, as well as non-significant variables that interact with the other items and provide the best AIC were retained. The

absence of multicollinearity between predictors was checked using the variance inflation factor. This led to the selection of the score variables. To simplify calculation, we allocated 1 point to each variable. We anticipated 3 prognostic levels of risk to identify a low-risk subgroup of patients who could be safely treated at home, an intermediate-risk subgroup who require hospitalization and a high-risk subgroup who may require intensive care. For defining low-risk patients, we chose the highest score value achieving a sensitivity of at least 0.90 and for defining high-risk patients, we chose the lowest score value achieving a specificity of at least 0.90.

Revised-HOME-CoV Score Validation The revised HOME-CoV score was validated in a validation cohort comprising patients with proven or probable COVID-19 during the interventional period of the original study. The discriminative ability of the score for both derivation and validation cohorts was assessed by calculating the Receiver Operating Characteristic (ROC) curve and analysing the Area Under the Curve (AUC). The AUC confidence interval was computed with the Delong-Delong method [19]. An AUC of ≥ 0.8 with a lower limit of the 95% confidence interval (95%CI) of ≥ 0.7 was considered clinically relevant. The Brier score was also reported, summarizing the magnitude of error in the probability forecasts between 0.0 and 1.0, where a perfect model has a score of 0.0 [20]. We also calculated the C-Index corresponding to the model discrimination. Calibration was assessed with the slope and the intercept value. Using the two predefined threshold values, sensitivity, specificity, likelihood ratios (LR) and the negative (NPV) and positive predictive values (PPV) with their 95% confidence interval (95%CI) of the revised HOME-CoV score were calculated.

Comparison of the clinical risk assessment models

In the validation cohort, we used .632+ bootstrapped logistic regression to evaluate the scores' performances and their confidence intervals and to assess performance against other scores: original HOME-CoV , qCSI, qSOFA, CRB65 and SMARTCOP. The comparison with CURB65 was performed in the subgroup of patients with uremia measured at baseline and the comparison with the SMART-COP in the subgroup of patients with pulmonary imaging. To calculate the SMART-COP, multi-lobar lesions on chest X-ray or CT scan were considered a positive criterion ("multi-lobar involvement on chest X-ray"). We report 95% confidence intervals derived from the percentiles of the bootstrapped distribution.

Complementary analyses

We performed a subgroup analysis in patients with confirmed SARS-CoV-2 infection by RT-PCR.

We also performed two sensitivity analysis with the following outcomes:

(1) Progression of illness as a function of time within the 28 days following ED presentation.

(2) Evolution to severe disease within 7 days, defined as requiring invasive ventilation or death whatever the cause (WHO-OSCI ≥ 6).

Statistical analysis

No imputation of missing data was done. If data were unavailable on the scores assessed, they were excluded from the individual analyses. Statistical analyses were performed using R software (version 3.5.1, R-Core Team) and the pec, timeROC, and survival R packages. [21,22].

RESULTS

A total of 3000 patients with confirmed or probable SARS-CoV-2 were included, 1696 patients in the derivation cohort and 1304 in the validation cohort (figure 1). Respectively, 65/1696 (3.8%) and 22/1304 (1.7%) patients had a progression of illness in the derivation and the validation cohorts. Patient characteristics are presented in Table 2.

HOME-CoV Score Revision

The Revised HOME-CoV score included 7 criteria (Table 3). The weighting of each criterion is shown in Table 3. The criterion “age over 65 years” was an independent factor for development of progression of illness within 7 days and its addition to the criteria of the original HOME-CoV score improved the performance of the score. Conversely, in the backward selection process, the criterion “systolic blood pressure < 90 mmHg”, “heart rate ≥ 120 bpm” and “severe comorbidity” were non-discriminatory and could be excluded without decreasing the revised score performance. The criteria “ability to talk without breathing < 8 seconds” positively impacted the model prediction. In the training cohort, the AUC of the revised HOME-CoV score was 87.6 (95% CI 84.7 to 90.6), with a C-Index of 86.6 and Brier score of 0.045 (Table 4). The AUC of the original HOME-CoV score was 80.9 (95% CI 76.3 to 85.6), with a C-Index of 80.5 and Brier score of 0.048.

The highest score achieving a sensitivity of at least 0.90 was < 2 for low-risk patients. For defining high-risk patients, the lowest score value that achieved a specificity of at least 0.90 was > 3 (Table 5).

In the subgroup of patients with confirmed SARS-CoV 2 infection (n=364 patients), the revised HOME-CoV score had an AUC of 83.7 (95% CI 78.6 to 88.7), a C-Index of 83.2 and a Brier score of 0.11 (Table 4).

Revised-HOME-CoV Score Validation

In the validation cohort, the AUC of the revised HOME-CoV score was 85.8 (95% CI 80.6 to 90.9), the Brier score was 0.019 and the C-Index was 85.71 to predict progression of illness within 7 days (Table 4). The calibration slope was 0.974 and the calibration intercept was -0.76 suggesting an over-estimation (Figure 2)(If the slope is close to 1 and the intercept is close to 0, then there is good overall calibration and good calibration across a range of risk groups.) Using a score value of < 2 as cut-off, 949/1304 (72.8%) qualified as low-risk patients and among them 5 had progression of illness, giving a sensitivity of 0.77 (0.55-0.92) and a NPV of 0.99 (0.99-1.00). There were 86/1304 (6.6%) patients with a score of > 3 qualified as high-risk patients. Among them, 12 developed severe illness yielding a specificity of 0.94 (0.93-0.96) and a PPV of 0.14 (0.07-0.23)) (Table 5). The two-by-two table is provided in table S2.

In the subgroup of patients with confirmed SARS-CoV 2 infection (n=183 patients), the revised HOME-CoV score had an AUC of 85.5 (95% CI 76.8 to 94.1) and a Brier score of 0.047 (Table 4). In this subgroup, 114/183 (62.3%) patients qualified as low-risk and among them, 1 had progression of illness for a sensitivity of 0.91 (0.59-1.00) and a NPV of 0.99 (0.95-1.00); 11/183 (6.0%) patients qualified as high-risk patients, and among them 3 had progression of illness with a specificity of 0.96 (0.92-0.98) and a PPV of 0.13 (0.05-0.32).

Comparison of the clinical risk assessment models

The predictive performance of the different scores within the 7 days of ED presentation are summarized in Table 4 and Table S3. The revised HOME-CoV score exhibited the

highest AUC in both cohorts and was significantly higher than that of the qSOFA, CURB65 and SMART-COP scores (table S3).

Complementary analyses

Time-dependent prediction

The AUC of the revised HOME-CoV score slightly decreased from Day 2 to Day 7 and was stable after Day 7: 85.8 (80.1-91.0) at Day 28 (Table 4, Figure S2).

Prediction of patients requiring intubation or dying within 7 days

Results regarding the rate of patients requiring intubation or who died within 7 days (WHO-OSCI ≥ 6) were similar to those above, with an AUC of the revised HOME-CoV of 86.7 (95%CI 84.6 to 91.8) (Table S4).

DISCUSSION

The revised HOME-CoV score includes 7 clinical criteria which can be assessed upon presentation to the ED. In our population, it exhibited good and stable over-time performance in predicting progression of illness in patients with suspected COVID-19 and in patients with confirmed COVID-19. Low-risk patients, eligible for home treatment, accounted for almost three quarters of the study population and less than 1% of this group required intensive care within the 28-day follow-up.

The revised and somewhat simplified HOME-CoV score exhibits non-significantly higher performances in risk characterization of progression of illness than the original version. Further, to facilitate its implementation in ED practice, biological variables and imaging data were not considered in the revised HOME-CoV score. The clinical variables are easy to assess upon presentation to the ED and enable rapid discharge

of low-risk patients. Moreover, the limited number of items and a simplified weighting makes the score easily memorable.

Many other risk-assessment scores have been proposed for COVID-19 patients [7–10,23–29]. Furthermore, their performance does not appear to be better than those of the revised HOME-CoV score [8,24]. We did not compare this score to the PRIEST score as we had not collected the performance status [9]. We also did not compare the revised HOME-CoV score with the NEWS2 generalist score because 154 patients were missing data for the temperature variable ~~for all patients~~ [30].

The revised HOME-CoV score was defined and validated in two cohorts of consecutive ED patients with suspected or proven non-severe COVID-19. Therefore, these datasets represent the target population that may benefit from its implementation as a decision-making tool [11]. The same positive performance was observed in the overall population and in the subgroup of patients with a positive RT-PCR for SARS-CoV2. This reinforces the validity of the score and its usability in EDs where access to RT-PCR for SARS-CoV2 is limited and/or where obtaining the results requires several hours [31]. As compared to the original score, the revised HOME-CoV score may increase the rate of patients managed at home without increasing their risk of death or requirement for intensive care. It could also be used by other frontline physicians such as general practitioners or geriatricians and help in mitigating the burden of COVID-19 on the healthcare system.

The patients included in the cohort were from the first wave of COVID-19. It is therefore possible that they are different from current patients who are mostly vaccinated and exposed to different variants. Indeed, fewer patients are getting worse due to less severe variants and vaccination but this does not mean that the signs of severity are different [4]. The severity of COVID-19 remains linked to the risk of respiratory failure

and this risk seems well assessed with items of the revised HOME-CoV score: pulse oxygen saturation ≤ 94% in ambient air, respiratory rate ≥ 25/min, ability to talk without breathing < 8 sec.

This study has several strengths. Analyses and results are based on a multicenter study with a large number of participating centers and patients and prospective data collection. We used a clinical and consensual main outcome based on the WHO criteria. This scale is more objective than other endpoints such as ICU admission or oxygen requirement.

It also has some limitations. Both cohorts came from the same centers. No calculation of the sample size was made a priori. The number of patients who met the endpoint was low, limiting the accuracy of the measurements. Comparison with physicians' gestalt would have been interesting, but this data was not collected. External validation has not been performed - the revised HOME-CoV score needs to be formally validated in a prospective implementation outcome study. We did not compare the revised HOME-CoV score with other scores such as the PRIEST or early warning scores (EWS). These tend to over-triage and require additional measured variables, whereas the aim of the revised HOME-CoV score is to be more discriminative and utilize variables available at presentation.

Implications

This revised HOME score allows stratification to determine which patients are at low risk and can be managed at home and which patients require hospitalisation due to risk of worsening. The use of this score is particularly relevant when the emergency physician is in situations of uncertainty and when resources are limited

CONCLUSIONS

The revised HOME-CoV score allows for accurate risk-stratification of patients presenting to emergency departments with proven or probable COVID-19 and appears comparable to most other scores. Future studies should evaluate its usefulness to frontline physicians in decision-making.

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Author Contribution

The DD, RJ, PA and PMR conceived, designed the study, managed the data. DD, FM, MR, CA, GS, FL, LR, SM, PG, BC, CC, MT, SD, PA, PMR collected data. RJ was the main statistician. RJ and DD conducted the statistical analyses. MR, DS served as scientific advisors. DD, FM, MR, CA, GS, FL, LR, SM, PG, BC, CC, MT, SD, PA, PMR discussed interpretation of data. The first draft of the manuscript was written by the DD, RJ and PMR. DD, RJ, FM, MR, CA, GS, FL, LR, SM, PG, BC, CC, MT, SD, PA, PMR contributed to the final manuscript and attest the accuracy of the data and the fidelity of the study to the protocol. DD is the guarantor and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Competing interest

None of the study authors have conflicts of interest to declare.

Statements on human and animal rights

The HOME-CoV study obtained approval from the Comité de Protection des Personnes Ouest IV – Nantes for France (N° 36/20_2), from the ethical committee of the Cliniques Universitaires Saint Luc (Bruxelles) for Belgium (N° 2020-A00831-38), and from the ethical committee Comité de Contrôle des Informations Nominatives of Monaco (N° 2020-069). This study was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

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Patient and public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research

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Table 1. Comparison between the different components of the risk assessment models.

Scores **Criteria**	Original HOME-CoV	qCSI	CURB 65	CURB 65	SMART-COP	qSOFA
Pulse oxygen saturation ≤94% in ambient air or need for oxygen therapy	✓	✓				
Respiratory rate (different cut-off, /min)	✓ (≥25)	✓ (≤22; 23-28;>28)	✓ (≥ 30)	✓ (≥ 30)	✓ (≥ 25)	✓ (≥ 22)
Ability to talk without breathing <8 seconds	✓					
Systolic blood pressure (different cut-off, mmHg)	✓ (≤ 90)		✓ (< 90)	✓ (< 90)	✓ (< 90)	✓ (≤ 100)
Heart rate (different cut-off, beats/min)	✓ (≥ 120)				✓ (≥ 125)	
Confusion or impaired consciousness	✓		✓	✓	✓	✓
Clinically significant worsening within the last 24 hours	✓					
Severe comorbidity* AND inadequate living conditions†	✓					
Age > 65 years			✓	✓	✓	
Oxygen Flow		✓				
Blood urea nitrogen > 19 mg/dL (> 7 mmol/L)			✓			
Albumin <3.5 g/dL (35 g/L)					✓	
PaO_2 <70 mmHg, SaO_2 ≤93%, or PaO_2/FiO_2 <333					✓	
PaO2/FiO2 Ratio < 250					✓	
Multi-lobar involvement on chest x-ray					✓	

* Severe chronic respiratory disease (unstable asthma, COPD stage III or IV, respiratory failure with continuous oxygen therapy), chronic heart failure (NYHA ≥ III), severe cognitive disorder, or immunodepression (primary immunodeficiency, uncontrolled HIV, immunosuppressive drug, chemotherapy).
† Inappropriate dwelling (homelessness, frail relative at home, long-term care institution), lack of support person (family member or friend), or home follow-up impossible.

Table 2. Baseline Characteristics of the Patients in the different cohorts

Characteristics	Derivation cohort		Validation cohort	
	Total	Confirmed COVID-19*	Total	Confirmed COVID-19*
	N=1696 (%)	N=346 (%)	N= 1304 (%)	N=183 (%)
Demographic characteristics				
Age – mean ± SD – yr	52.2 ±19.9	55±17.9	52.5 ± 18.5	53±16.3
Female sex – no. (%)	918 (54.1)	186 (53.8)	725 (55.6)	114 (62.3)
Medical history – no. (%)				
Severe cognitive impairment	18 (1.1)	7 (2.0)	6 (0.5)	2 (1.1)
COPD stage III/IV	34 (2.0)	5 (1.4)	22 (1.7)	0 (0)
Asthma	176 (10.4)	28 (8.1)	147 (11.3)	17 (9.3)
Severe renal disease (GFR < 30ml/min)	37 (2.2)	10 (2.9)	28 (2.1)	5 (2.7)
Hepatic cirrhosis child B or C	10 (0.6)	1 (0.3)	7 (0.5)	3 (1.6)
Chronic cardiac failure NYHA III/IV	24 (1.4)	1 (0.3)	18 (1.4)	6 (3.3)
Hypertension	518 (30.5)	135 (39.0)	351 (26.9)	53 (29.0)
Diabetes	221 (13.0)	64 (18.5)	141 (10.8)	28 (15.3)
History of thromboembolism	94 (5.5)	13 (3.8)	68 (5.2)	10 (5.5)
Cancer history or active cancer	159 (9.4)	35 (10.1)	115 (8.8)	19 (10.4)
Immune deficiency and HIV	55 (3.2)	14 (4.0)	33 (2.5)	11 (6.0)
Signs and symptoms – no. (%)				
Anosmia, ageusia, dysgeusia	400 (23.6)	112 (32.4)	243 (18.6)	47 (25.7)
Cough	1127 (66.5)	271 (78.3)	853 (65.4)	117 (63.9)
Dyspnea	1094 (64.5)	244 (70.5)	769 (59.0)	97 (53.0)
Diarrhea	445 (26.2)	81 (23.4)	350 (26.8)	38 (20.8)
Chest pain	592 (34.9)	82 (23.7)	463 (35.5)	57 (31.1)
Confusion, impaired alertness	91 (5.4)	35 (10.1)	44 (3.4)	8 (4.4)
Worsening in the last 24 hours	842 (49.6)	203 (58.7)	515 (39.5)	77 (42.1)
Heart rate ≥ 120 beats/min	88 (5.2)	23 (6.7)	76 (5.8)	9 (4.9)
Systolic blood pressure < 90 mmHg	12 (0.7)	3 (0.9)	7 (0.5)	2 (1.1)
Body Mass Index ≥ 30 kg/m^2	230 (13.6)	57 (16.5)	197 (15.1)	32 (17.5)
Pulse oxygen saturation ≤94% in ambient air or necessity of oxygen therapy	381 (22.5)	121 (35.0)	326 (25.0)	42 (23.0)
Respiratory rate ≥ 25/min	302 (17.8)	55 (15.9)	184 (14.1)	36 (19.7)
Ability to speak or count without resuming breathing < 8 seconds	206 (12.1)	38 (11.0)	93 (7.1)	21 (11.5)
COVID-19 status				
Typical COVID-19 lesion on CT scan	341 (20.1)	182 (52.6)	240 (18.4)	50 (27.3)
Adverse evolution within the 7 days	65 (3.8)	41 (11.8)	22 (1.7)	9 (4.9)

Requiring non-invasive ventilation	18 (1.1)	12 (3.5)	10 (0.8)	5 (2.7)
Requiring mechanical ventilation	15 (0.9)	11 (3.2)	4 (0.3)	2 (1.1)
Death (all causes)	32 (1.9)	18 (5.2)	8 (0.9)	2 (1.1)

COPD: Chronic Obstructive Pulmonary Disease; NYHA: New York Heart Association; HIV: Human Immunodeficiency Virus; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction; CT-Scan: Computerized Tomography scanner.
* Confirmed SARS-CoV-2 infection by Reverse Transcriptase-Polymerase Chain Reaction.

Table 3. Revised HOME-CoV score.

The presence of one or more criteria corresponds to a patient at risk of pejorative evolution and should lead the physician to consider hospitalization:	**Points**
Age > 65 years	1
Pulse oxygen saturation ≤ 94% in ambient air	1
Respiratory rate ≥ 25/min	1
Ability to talk without breathing < 8 sec	1
Confusion or impaired consciousness	1
Clinically significant worsening within the last 24 hours	1
Inadequate living conditions[†]	1

[†] Inappropriate dwelling (homelessness, frail relative at home, long-term care institution), lack of support person (family member or friend), or home follow-up impossible.

Table 4. Performance scores in the derivation and validation cohorts over time.

Derivation Cohort (n=1696)	At D2		At D7		At D28	
	AU-ROC (95% bootstrap CI)	Brier score	AU-ROC (95% bootstrap CI)	Brier score	AU-ROC (95% bootstrap CI)	Brier score
Revised HOME-CoV	89.3 (86.9-91.7)	0.036	87.6 (84.7-90.6)	0.045	86.7 (83.5-89.9)	0.047
Original HOME-CoV	81.4 (76.6-86.2)	0.043	80.9 (76.3-85.6)	0.048	80. 7 (76.2-85.1)	0.049
qCSI	76.9 (71.6-82.1)	0.038	75.5 (70.6-80.5)	0.044	74.7 (69.7-79.7)	0.045
qSOFA	75.6 (70.3-80.8)	0.042	74.4 (69.4-79.3)	0.049	73.0 (68.1-78.0)	0.050
CRB65	83.9 (79.9-88.0)	0.038	78.6 (73.7-83.5)	0.044	77.8 (72.9-82.6)	0.045
Validation Cohort All patients (n=1304)	At D2		At D7		At D28	
	AU-ROC (95% bootstrap CI)	Brier score	AU-ROC (95% bootstrap CI)	Brier score	AU-ROC (95% bootstrap CI)	Brier score
Revised HOME-CoV	86.5 (81.1-91.9)	0.018	85.8 (80.6-91.0)	0.019	85.8 (80.6-91.0)	0.019
Original HOME-CoV	85.1 (78.9-91.4)	0.021	84.2 (78.4-90.0)	0.022	84.2 (78.4-90.0)	0.022
qCSI	79.0 (70.8-87.2)	0.021	78.7 (70.9-86.5)	0.022	78.7 (70.9-86.5)	0.022
qSOFA	70.4 (61.6-79.31	0.021	71.9 (64.00-79.7)	0.023	71.9 (64.0-79.7)	0.023
CRB65	77.3 (68.8-85.8)	0.021	77.6 (69.5-85.8)	0.022	77.6 (69.5-85.8)	0.022
Validation Cohort Confirmed COVID-19* (n=183)	At D2		At D7		At D28	
	AU-ROC (95% bootstrap CI)	Brier score	AU-ROC (95% bootstrap CI)	Brier score	AU-ROC (95% bootstrap CI)	Brier score
Revised HOME-CoV	87.8 (81.2-94.4)	0.039	85.5 (76.8-94.1)	0.047	85.5 (76.8-94.1)	0.030
Original HOME-CoV	85.2 (76.4-93.9)	0.050	83.4 (75.0-91.9)	0.062	83.4 (75.0-91.9)	0.046
qCSI	73.6 (56.2-91.1)	0.045	74.1 (58.4-89.9)	0.042	74.1 (58.4-89.9)	0.051
qSOFA	69.9 (51.8-88.0)	0.055	71.8 (58.3-85.3)	0.059	71.8 (58.3-85.3)	0.053
CRB-65	76.2 (63.2-89.3)	0.051	75.5 (62.2-88.7)	0.059	75.4 (62.2-88.7)	0.053

* Confirmed SARS-CoV-2 infection by Reverse Transcriptase-Polymerase Chain Reaction.
AU-ROC : Area under the curve of receiver operating characteristic, Ci : Confidence interval, qCSI : quick COVID severity Index, qSOFA: quick Sequential Organ Failure Assessment.

Table 5. Distribution of the revised HOME-CoV score among patients according to different threshold in training and validation cohorts.

All patients (N=3000)	Training cohort (n=1696)		Validation cohort (n=1304)	
Defined threshold	**< 2** (n=1092, 64.4%)	**> 3** (n= 158, 9.3%)	**< 2** (n= 949, 72.7%)	**> 3** (n= 86, 6.6%)
Performances (95% CI)				
Sensitivity	0.96 (0.89-0.99)	0.44 (0.34-0.55)	0.77 (0.55-0.92)	0.56 (0.32-0.76)
Specificity	0.65 (0.63-0.68)	0.93 (0.92-0.94)	0.74 (0.71-0.76)	0.94 (0.93-0.96)
Negative predictive value	1.00 (0.99-1.00)	0.97 (0.96-0.98)	0.99 (0.99-1.00)	0.99 (0.98-0.99)
Positive predictive value	0.13 (0.11-0.16)	0.26 (0.19-0.34)	0.04 (0.04-0.06)	0.14 (0.07-0.23)
Negative likelihood ratio	0.07 (0.03-0.17)	0.60 (0.50-0.72)	0.31 (0.14-0.67)	0.48 (0.31-0.76)
Positive likelihood ratio	2.77 (2.56-2.99)	6.29 (4.72-8.39)	2.93 (2.30-3.74)	9.45 (6.08-14.69)
Confirmed COVID-19* (n=183)	Training cohort (n=346)		Validation cohort (n=183)	
Defined threshold	**< 2** (n=199, 57.5%)	**> 3** (n=31, 9.0%)	**< 2** (n=114, 62.3%)	**> 3** (n=11, 6.0%)
Performances (95% CI)				
Sensitivity	0.96 (0.87-1.00)	0.46 (0.31-0.62)	0.91 (0.59-1.00)	0.56 (0.34-0.72)
Specificity	0.60 (0.54-0.65)	0.94 (0.90-0.96)	0.66 (0.58-0.73)	0.96 (0.92-0.98)
Negative predictive value	0.99 (0.96-1.00)	0.96 (0.95-0.99)	0.99 (0.95-1.00)	0.99 (0.95-1.00)
Positive predictive value	0.28 (0.22-0.35)	0.34 (0.11-0.42)	0.14 (0.07-0.25)	0.13 (0.05-0.32)
Negative likelihood ratio	0.06 (0.02-0.24)	0.58 (0.45-0.74)	0.99 (0.95-1.00)	0.58 (0.41-0.80)
Positive likelihood ratio	2.38 (2.07-2.74)	7.42 (3.82-8.45)	2.65 (2.01-3.50)	7.96 (5.01-14.21)

* Confirmed SARS-CoV-2 infection by Reverse Transcriptase-Polymerase Chain Reaction.

CI: Confidence Interval