Validation of the revised HOME-CoV rule to safely discharge patients with COVID-19: a multicenter prospective cohort

Validación de la regla HOME-CoV revisada para dar de alta de forma segura a pacientes con COVID-19 en una cohorte prospectiva multicéntrica

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The SARS-CoV-2 pandemic has pushed health systems around the world to their limits. For Emergency Departments (EDs), early identification of COVID-19 patients who can be safely managed at home has become a major issue in retaining the capacity for care for patients at risk of worsening in the coming days.[1] Using a Delphi method, we previously constructed and prospectively validated the HOME-CoV rule (Hospitalization or Outpatient ManagEment of patients with SARS-CoV-2 infection).[2,3] To optimize this initial rule, a derivation and validation model was performed using the database of the validation trial (Douillet et al., under review). The revised HOME-CoV score included 7 criteria (Table 1) and, retrospectively, exhibited good performances (AUC 87.6 - 95% confidence interval (CI): 84.7 to 90.6).

The aim of the present trial was to prospectively validate the revised HOME-CoV score in identifying a subgroup of ED patients with a low risk of adverse evolution who could be safely treated at home.

The revised-HOME-CoV study was a pragmatic prospective multicenter implementation trial conducted in the EDs of 30 European hospitals. The primary objective was to demonstrate the safety of home treatment for COVID-19 patients with a revised HOME-CoV score < 2. The primary endpoint was the rate of adverse outcomes defined as use of high-flow nasal oxygen therapy, non-invasive or invasive ventilation, or all-cause death within 7 days of ED admission. A rate of less than or equal to 0.5% with an upper limit of the 95%CI to 1% or less was a priori set to consider the revised HOME-CoV score as reliable. Considering an overall prevalence of adverse outcome of 5%, a rate of patients with a score < 2 of 40%, an alpha risk of 5%, and a power of 80%, the required number of inclusions was 1232 patients.

Table 1. Original and Revised HOME-CoV scores

The presence of one or more criteria corresponds to a patient at risk of pejorative evolution and should lead the physician to consider hospitalization:	Original HOME-CoV score	Revised HOME-CoV score
Age > 65 years	-	1
Pulse oxygen saturation ≤ 94% in ambient air	1	1
Respiratory rate ≥ 25/min	1	1
Ability to talk without breathing < 8 sec	1	1
Confusion or impaired consciousness	1	1
Clinically significant worsening within the last 24 hours	1	1
Inadequate living conditions†	–	1
Severe comorbidity* AND inadequate living conditions†		
Heart rate ≥ 120 beats/min	1	–
Systolic blood pressure ≤ 90 mmHg	1	–
Positivity threshold	**≥ 1**	**≥ 2**

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

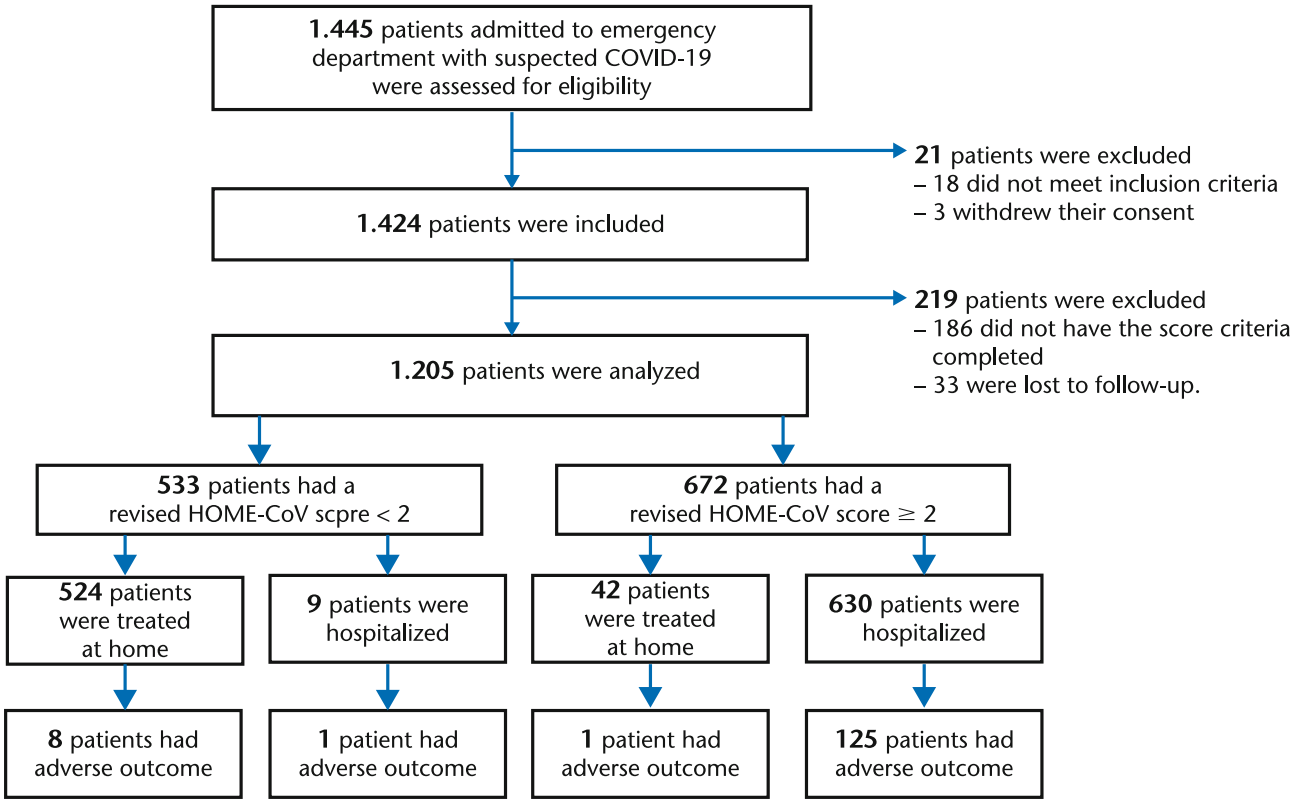

Figure 1. Flowchart.

Patients were eligible for inclusion if they provided informed consent, were at least 18 years old, and had a symptomatic case of COVID-19. They were excluded if the main diagnostic hypothesis in the ED was not a SARS-CoV-2 infection, if they required intensive care, if their personal liberty was limited, or if follow-up at Dday 7 was not possible.

The revised HOME-CoV score was implemented in participating centers using telephone meetings, posters, and pocket cards. Patients were selected for home treatment if the score was < 2 and for hospitalization otherwise. Nevertheless, the physician-in-charge could overrule this qualification in the case of imperative medical or social reasons. Patients or relatives were contacted with a standardized phone interview at Dday 7 after inclusion, at which point their clinical status was recorded.[4]

Statistical analyses were performed using R software (version 3.5.1, R-Core Team). The study obtained ethical approval on November 20, 2020 (ID-RCB:2020-A03067-32) and was sponsored and funded by the CHU Angers. The trial registration number was NCT04657471.

A total of 1445 patients were included from 08 December 2020 to 22 March 2021 and data pertaining to 1205 were analyzed (figure 1). Patients' characteristics are summarized in table 2. At day 7, 135 (11.2%, 95%CI 9.5 – 13.1) patients had an adverse evolution, of whom 59 (4.9%, 95%CI 3.8 – 6.3) required mechanical ventilation and 31 died (2.6%, 95%CI 1.8 – 3.6). In the whole population, the rate of outpatients was 47.0% (95%CI 44.2 - 49.8, n = 566/1205) (Figure 1).

A total of 533 (44.2%) patients had a revised HOME-CoV score < 2 and 9 of them had an adverse evolution (n = 9/533, 1.7%, 95%CI 0.9 – 3.2). In this subgroup, 524 (98.3%) patients were treated at home and 8 of them had an adverse evolution (n = 8/524, 1.5%, 95%CI 0.8 – 2.9). The HOME-CoV score was ≥ 2 in 672 (55.8%) patients and 126 of them had an adverse evolution (n=126/672, 18.8%, 95%CI 16.0 – 21.9).

The revised HOME-CoV score AUC was 0.78 (95%CI 0.76 – 0.82). The performances with a threshold fixed at 2 were 93.3 (95%CI 87.7 – 96.9), 49.0 (95%CI 46.0 – 52.0), 18.6 (95%CI 17.5 – 19.7), and 98.3 (95%CI 96.9 – 99.1) for sensibility, specificity, and positive and negative predictive values, respectively.

For the initial HOME-CoV score, 375 (31.1%) patients had a score = 0 (negative rule), of whom 39 (10,4%, 95%CI 7.7 – 13.9) had an adverse outcome at D7. The AUC of the initial HOME-CoV score was 0.72 (95%CI 0.67 – 0.76). The sensitivity, specificity, and positive and negative predictive values were 71.1 (95%CI 62.7 – 78.6), 31.4 (95%CI 28.6 – 34.3), 11.5 (95%CI 10.3 – 12.7), and 89.7 (95%CI 86.8 – 92.0), respectively.

The revised-HOME-CoV score enables the identification of a large subgroup of patients at low risk of evolution toward severe COVID-19. However, the rate of adverse outcome in patients with a revised-HOME-CoV score < 2 was higher than the expected and predefined safety cutoff (1.7% versus 0.5%). Similarly, the initial HOME-CoV score exhibited performances much lower than previously observed, whereby 10% of patients with a negative rule experienced an adverse outcome.[2,3]

This discrepancy may be explained by the evolution of care in patients with COVID-19. In contrast to the beginning of the pandemic when the first HOME-CoV trial was performed, today, many patients with pauci-symptomatic and/or minor COVID-19 are managed in primary care. As a result, COVID-19 patients who presented to ED had a

Table 2. Characteristics of patients with an adverse evolution at 7 days

	Total N = 1205 n (%)	Adverse evolution N = 135 n (%)	No adverse evolution N = 1070 n (%)
Demographic characteristics			
Age [Mean (SD)] (years)	63 (19)	75 (12)	59 (15)
Female sex	573 (62.5)	36 (26.7)	537 (50.2)
Medical history			
Severe cognitive impairment	7 (0.6)	1 (0.7)	6 (0.6)
COPD stage III/IV	21 (1.7)	2 (1.5)	19 (1.8)
Chronic respiratory failure	13 (1.1)	3 (2.2)	10 (0.9)
Controlled or unstable asthma	85 (7.1)	3 (2.2)	82 (7.7)
Severe or end-stage renal disease (GFR < 30 ml/min)	29 (2.4)	8 (5.9)	21 (2.0)
Hepatic cirrhosis child B or child C	4 (0.3)	1 (0.7)	3 (0.3)
Chronic cardiac failure NYHA III/IV	17 (1.4)	4 (3.0)	13 (1.2)
Hypertension	494 (41.0)	81 (60.0)	413 (38.6)
Diabetes	221 (18.3)	42 (31.1)	179 (16.7)
History of thromboembolism	73 (6.1)	10 (7.4)	63 (5.9)
Historic or active cancer	129 (10.7)	24 (17.8)	105 (9.8)
Immune deficiency and HIV	26 (2.2)	1 (0.7)	25 (2.3)
Inadequate living conditions	79 (6.6)	31 (23.0)	48 (4.5)
Signs and symptoms			
Anosmia, ageusia, dysgeusia	256 (21.2)	18 (23.0)	238 (22.2)
Cough	816 (67.7)	90 (13.3)	726 (67.9)
Dyspnea	779 (64.6)	114 (84.4)	665 (62.1)
Diarrhea	306 (25.4)	32 (23.7)	274 (25.6)
Chest pain	247 (20.5)	9 (6.7)	238 (22.2)
Confusion, impaired alertness	43 (3.6)	11 (8.1)	32 (3.0)
Worsening in the last 24 hours	678 (56.3)	110 (81.5)	568 (53.1)
Heart rate ≥ 120 beats/min	54 (4.5)	8 (5.9)	46 (4.3)
Systolic blood pressure < 90 mmHg	4 (0.3)	1 (0.7)	3 (0.3)
Temperature [Mean (SD)] (°C)	37.2 (1)	37.1 (1)	37.2 (1)
Body mass index ≥ 30kg/m^2	228 (18.9)	28 (20.7)	200 (18.7)
Pulse oxygen saturation ≤ 94% in ambient air or necessity of oxygen therapy	527 (43.7)	110 (81.5)	417 (39.0)
Respiratory rate ≥ 25/min	283 (23.5)	59 (43.7)	224 (20.9)
Ability to speak or count without resuming breathing < 8 seconds	229 (19.0)	45 (33.3)	184 (17.2)

*An adverse evolution is defined by the use of high-flow nasal oxygen therapy, non-invasive or invasive ventilation, or all-cause death within 7 days of ED admission.

higher risk of adverse outcome: 11% in the present trial versus 2% in the first one.[2,3] Many severity scores have been developed for COVID-19 patients but mainly with the objective of predicting which patients will require intensive care.[5-9] To our knowledge, the initial and revised HOME-CoV scores are the first scores prospectively validated aiming to assess safe home treatment. The initial HOME-CoV score was based on an expert consensus and was statistically reworked on a large prospective database to perform the revised HOME-CoV score. This methodology, based on the selection of relevant variables by clinicians followed by a statistical derivation in a parsimonious way, is considered as the best way for constructing scores.[5] Our results confirm this approach, the performance of the revised HOME-CoV score being much better than the initial HOME-CoV score.[2,3] In the current context, the revised HOME-CoV score is relevant despite vaccination and the different variants because the symptoms of severity remain similar.

To conclude, the revised HOME-CoV score exhibits good performance. It is based on only 7 clinical items that are easy to assess, even by phone, and it can be a helpful tool for frontline and emergency physicians to triage COVID-19 patients for home treatment.

Addendum

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