

Outpatient Management of Patients With COVID-19: Multicenter Prospective Validation of the Hospitalization or Outpatient Management of Patients With SARS-CoV-2 Infection Rule to Discharge Patients Safely

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Outpatient Management of Patients With COVID-19: Multicenter Prospective Validation of the HOME-CoV Rule to safely discharge patients.

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ABSTRACT

Background

The HOME-CoV rule is a checklist of eligibility criteria for home treatment of patients with COVID-19, defined using a Delphi method.

Research Question

Is the HOME-CoV rule reliable for identifying a subgroup of COVID-19 patients with a low risk of adverse outcomes who can be safely treated at home?

Study Design and Methods

We aimed to validate the HOME-CoV rule in a prospective multicenter study before and after trial on patients with probable or confirmed COVID-19 who presented at the emergency departments (ED) of 34 hospitals. The main outcome was an adverse evolution, i.e., invasive ventilation or death, occurred within the 7 days following the patients' admission. The performance of the rule was assessed by the false negative rate. The impact of the rule implementation was assessed by the absolute differences in the rate of patients who required invasive ventilation or who died and in the rate of patients treated at home, between an observational and an interventional period after implementation of the HOME-CoV rule, with propensity score adjustment.

Results

Among 3000 prospectively enrolled patients, 1239 (41.3%) had a negative HOME-CoV rule. The false negative rate of the HOME-CoV rule and its AUC were 4/1239: 0.32% (95%CI: 0.13 to 0.84%) and 80.9 (95%CI: 76.5 to 85.2), respectively. On the adjusted populations, 25/1274 (1.95%) patients experienced an adverse evolution during the observational period versus 12/1274 (0.95%) during the interventional period: -1.00 (95%CI: -1.86 to -0.15). During the observational period, 858 (67.35%) patients were treated at home versus 871 (68.37%) patients during the interventional period: -1.02 (95%CI -4.46 to 2.26).

Interpretation

A large proportion of ED patients with probable or confirmed COVID-19 have a negative HOME-CoV rule and can be safely treated at home with a very low risk of complication.

Clinical Trial Registration Number: NCT04338841

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The COVID-19 pandemic leads to significant increases in the demand for hospital beds and a shortage of medical equipment. In order to mitigate the burden on the healthcare system, while also providing the best possible care for patients, the emergency physicians have to identify low-risk patients who can be treated at home and high-risk patients who require hospitalization and, in some cases, admission to an intensive care unit.

Several risk assessment models for COVID-19 have emerged [1–4] and pre-existing scores designed for pneumonia or sepsis were also evaluated for this purpose [5,6]. However, all these models seem to be at high risk of bias and none has been validated in an implementation study [7]. Moreover, all of them have been based on hospitalized patients and focused on the assessment of severity rather than the identification of a subgroup of low-risk patients presenting to the Emergency Department (ED) and who can be safely discharged home [7]. Finally, for many ED patients with suspected COVID-19, the decision between hospitalization and home discharge needs to be made without waiting for biological confirmation with a positive Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) for SARS-CoV2.

Using a Delphi method, we previously developed the HOME-CoV Rule aiming to help physicians in triaging patients with confirmed or probable COVID-19 for home treatment [8]. Eight clinical criteria precluding home treatment were selected, the HOME-CoV Rule being deemed negative allowing home discharge if none of them is met (Table 1).

In order to prospectively validate the HOME-CoV rule, we performed a pragmatic before/after study and hypothesized that the implementation of the HOME-CoV rule will be at least as safe as previous and current practices with regard to the rate of patients with an adverse evolution at Day 7 and will lead to a higher rate of patients being managed at home.

METHODS

Study Design

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The HOME-CoV study was a pragmatic prospective multicenter before/after design trial conducted in the ED of 34 hospitals: 31 in France, 2 in Belgium and one in the Principality of Monaco (e-Appendix 1).

Selection of Participants

Patients were eligible for inclusion if they provided informed consent, were at least 18 years old, and had a symptomatic COVID-19 confirmed by a positive SARS-CoV-2 RT-PCR or COVID-19 was the most likely hypothesis according to the physician in charge of the patient. Patients were excluded if they required care in an intensive care unit or in a resuscitation unit, if a limitation decision of active therapies was made, if follow-up at Day 28 would not be possible, and if they were an individual deprived of liberty by a judicial or administrative decision, under psychiatric care under duress, under a legal protection measure, or unable to express consent.

Study procedures

The first period was observational and the decision between hospitalization and home treatment was left up to the emergency physicians according to their current practices. A transition period without inclusion of 4 days allows the HOME-CoV rule to be implemented in participating centers using telephone meetings, posters, and pocket cards (e-Appendix 2). During the interventional period, the physicians had to apply the HOME-CoV rule. Patients were selected for home treatment if all criteria were negative, and for hospitalization otherwise (Table 1). The physician-in-charge could overrule this qualification in the case of imperative medical or social reasons.

During the two periods, data were prospectively collected. Patients were followed with a standardized phone interview at Day 7 and Day 28 after inclusion in the study and their clinical status was recorded, using the Ordinal Scale for Clinical Improvement for COVID-19 patients from the World Health Organization (WHO-OSCI)[9] (e-Appendix 3). The date of each change in the WHO-OSCI status, and especially the date of intubation, if applicable, was also recorded to allow analysis over time.

Methods of Measurement and Outcome Measures

HOME-CoV Rule Performance

The performance of the rule was assessed by the rate of patients with evolution to a severe COVID-19 according to the WHO-OSCI definition (stages 6 to 8), i.e., requiring invasive ventilation and/or

dying, among patients with a negative HOME-CoV rule within the 7 days following their inclusion (false negative rate). The area under the receiving operating curve (AUC), sensitivity, specificity, negative and positive predictive value, and negative and positive likelihood ratio were also calculated. A complementary analysis was performed at 28-day follow-up and a subgroup analysis was performed in patients with a positive RT-PCR for SARS-CoV-2.

Implementation of the HOME-CoV Rule

The impact of the implementation of the HOME-CoV rule was assessed by comparison between the observational period and the interventional period after adjustment using a weighting-based propensity score. The primary safety outcome was the rate of patients having invasive ventilation or dying within the 7 days after inclusion. The primary efficacy outcome was the rate of patients treated at home, defined as patients discharged home within 24 hours following their presentation at ED.

We performed subgroup analysis in patients treated at home and with a negative or a positive HOME-CoV rule and in hospitalized patients and with a negative or a positive HOME-CoV rule.

We performed sensitivity analyses with the following outcomes:

- an adverse evolution (i.e., invasive ventilation or death) within 28 days following inclusion.
- a poor outcome defined as a patient hospitalized and requiring at least oxygen support (stages 4 to 8 of the WHO-OSCI) within 7 days of inclusion.

Statistical Analysis

For descriptive analyses, quantitative variables were reported as mean ± standard deviation (SD) when their distribution can be considered as Gaussian, and with median and inter quartile ranges (IQR) otherwise. Qualitative variables were reported using numbers and proportions. Comparisons were performed using Student or Mann-Whitney tests for quantitative variables and using the Fisher Exact test for qualitative variables. We used a predefined threshold of ≥1 and considered that the upper limit of the 95% confidence interval (95%CI) of the false negative rate should be lower than 2% for validation of the HOME-CoV rule [10].

For comparison between the observational period and the interventional period, weighting-based propensity scores (Inverse Probability Weighting) were used to account for individual profile

differences between the two periods. All major variables available at the time of ED presentation were considered in the model (e-Figure 1). Once the patient profiles had been balanced between the two phases, a logistic regression was performed that included a random effect on the center enabling computation of the confidence interval for the difference in event rates between the two periods [11,12]. We used a hierarchical approach. The first step was a non-inferiority (one-sided) analysis on the primary safety outcome (i.e., adverse evolution with invasive ventilation or death) with a pre-specified non-inferiority margin of 2%. The second step was a superiority analysis (two sided) on the rate of patients treated at home. P<0.05 was considered as statistically significant.

The compliance with the HOME-CoV rule defined as the proportion of patients with a negative HOME-CoV rule who were actually treated at home after ED presentation was also assessed.

The hierarchization of objectives allowed us to avoid the problem of multiplicity as much as possible. No imputation of missing data was performed [13]. Descriptive analysis of these data was performed using the naniar package and compared to no missing data in order to consider a potential bias.

Considering a non-inferiority margin of 2% and a 5% incidence rate of the primary endpoint in each period, and assuming a dropout rate of 5%, 1542 patients per study period were needed to achieve 80% power using a one-sided alpha level of 5% [14]. Statistical analyses were performed using R software (version 3.5.1, R-Core Team) and the following R package: pec, WeigthIt packages and Survey [15].

Ethical Considerations

The HOME-CoV study obtained approval from the "Comité de Protection des Personnes Ouest IV – Nantes" on March 4, 2020 (N°36/20_2) for France, from the ethical committee of Cliniques Universitaires Saint Luc for Belgium (N°2020-A00831-38), and from the "Commission des Contrôles des Informations Nominatives" of Monaco (N° n° 2020-069). The study was sponsored and funded by the CHU Angers. The funding source had no role in data collection, data analysis, data interpretation, or writing of the report. The trial was carried out in accordance with the principles of the Declaration of Helsinki and the Good Clinical Practice guidelines. The trial registration number was NCT04338841.

RESULTS

Characteristics of the Patients

A total of 3133 patients with confirmed or probable SARS-CoV-2 infection were prospectively enrolled, 1763 during the observational period from April 9 to April 18, 2020 and 1370 during the interventional period from April 21 to May 11, 2020. The capacity rate of intensive care units in France was 106% and 99% during the first and the second period, respectively. Among the patients included, 3000 completed Day 7 follow-up and 133 (1.02%) were lost to follow-up (no significant difference between the two periods) (Figure 1). Patients' characteristics at baseline are presented in Table 2. The median age was 53.4 years, and 54.5% of patients were women. The median time between the onset of symptoms and the ED visit was 5 days (IQR 2-12) and 45% (n=1409) of the patients had a clinically significant worsening within the last 24 hours. Inadequate living conditions were observed in 414 (13.8%) patients: 186 patients with inappropriate dwelling (homeless, frail relative at home, long term care institution), 245 patients without support person, 55 patients for whom follow-up was not possible, 66 patients having several criteria of inadequate living conditions. COVID-19 was confirmed by RT-PCR for SARS-CoV-2 in 529 patients (e-Table 1). CT scans reported strong evidence of COVID-19 infections in 581 patients, 234 patients having a positive RT-PCR and a chest CT scan suggestive of COVID-19. After ED assessment, 2066 patients were treated at home (65.94%) and among them, 36 were secondarily admitted to hospital within the 7 days following their inclusion in the trial (1.74%). Among hospitalized patients (n=1067/3133, 34.06%), 491 (46.02%) were still hospitalized at Day 7. In the overall population within the 7 days following ED presentation, 223 (7.4%) required oxygen therapy, 28 (0.9%) non-invasive ventilation, and 57 (1.9%) patients met the primary outcome: 19 (0.6%) had required intubation and invasive ventilation and 38 (1.3%) were dead. At Day 28, 85/2912 patients (2.9%) had experienced an adverse evolution, 5 (0.2%) had been intubated and 80 (2.7%) were dead (e-Table 2).

HOME-CoV Rule Performance

In the overall population, 1239/3000 (41.3%) patients had a negative HOME-CoV rule. Among them, 3 patients required intubation and invasive ventilation and one patient died within the 7 days after ED presentation (n=4/1239) (Table 3). The false negative rate of the HOME-CoV rule was 0.32% (95%CI: 0.13 to 0.84%) meeting the predefined threshold of the upper limit of the 95% confidence interval (<2%). The AUC was 80.9 (95%CI: 76.5 to 85.2). At Day 28, the AUC was 80.65 (95%CI 76.41 to 84.88). Six patients out of the 1239 patients with an initial negative HOME-CoV rule had an adverse evolution within the 28-day follow-up. The false negative rate was 0.48 (95%CI: 0.22 to 1.08). In the subgroup of patients with a positive SARS-CoV-2 RT-PCR (n=529), the AUC was 78.47 (95%CI: 74.79 to 86.19) at Day 7. The false negative rate of the HOME-CoV rule in this subgroup was 0.28% (95%CI: 0.05 to 1.58%).

Implementation of the HOME-CoV Rule

After using a weighting-based propensity score and excluding patients who could not be assessed at Day 7, 1274 patients were included in the adjusted population of each period (Table 2). Patients' characteristics were similar between the two periods (Table 2). The evolution of the patients according to the WHO-OSCI is noted in Figure 2.

In the adjusted population, 12 patients (0.95%) underwent an adverse evolution at Day 7 during the interventional period versus 25 (1.95%) patients during the observational period. The absolute difference was -1.00 (CI95%: -1.86-to -0.15), meeting the non-inferiority pre-defined criterion ($p<0.01$ for non-inferiority) and showing a statistically significant difference in favor of the interventional period ($p=0.004$ for superiority). The difference between the two periods mainly depends on the difference observed in the subgroup of hospitalized patients with a positive HOME-CoV rule: -4.4 (95%CI: -5.7 to -2.4) (Table 4). In the adjusted population, during the interventional period 89.3% (560/627) of patients with a negative HOME-CoV rule were treated at home and none of them was subsequently hospitalized.

During the interventional period, 871 (68.38%) patients were treated at home versus 858 (67.33%) patients during the observational period without significant absolute difference: -1.02 (95%CI: -4.46 to 2.26). During the interventional period, the compliance to the HOME-CoV rule was 90% (n=618/687)

and more patients with a negative HOME-CoV rule were treated at home than during the observational period: +7.2 (95%CI: 3.3 to 11.1) (Table 4).

Sensitivity Analyses

At Day 28 on the adjusted population, 21/1235 (1.7%) patients experienced an adverse evolution during the interventional period versus 40/1232 (3.2%) during the observational period. The absolute difference was -1.5 (95%CI: -0.4 to -2.6).

The results were similar when using the rate of poor outcome at Day 7 as a judgment criterion, i.e., patients requiring oxygen therapy or non-invasive or invasive ventilation or who had died (e-Table 3).

DISCUSSION

This prospective multicentric study validates the HOME-CoV rule as a helpful tool in deciding whether to opt for home treatment in ED patients with confirmed or probable COVID-19. A negative HOME-CoV rule qualified a large subgroup of patients at very low risk of adverse outcome. The rate of patients who required invasive ventilation or who died within the 7 days following ED presentation was lower with HOME-CoV rule implementation than in the previous observational period. More than two thirds of patients were treated at home without significant difference between the two periods.

Several risk-stratification models are proposed for COVID-19 patients[8]. The goal of most of them is to identify high-risk patients requiring intensive care, i.e., the Quick-COVID Severity Index, the COVID-GRAM score, and the score developed by Xie et al[1,16,17]; and all of these were based on hospitalized patients with COVID-19. As the Pulmonary Severity Index for patients with community-acquired pneumonia,[18] the HOME-CoV rule was specifically designed to help emergency physicians in deciding whether to opt for home treatment over hospitalization in COVID-19 patients. Moreover, as in the ED, the result of the SARS-CoV2 RT-PCR was unknown for many patients with suspected COVID-19; patients with typical signs of COVID-19 were therefore included provided that the physician considered COVID-19 as the main diagnostic hypothesis. Although testing has become widespread, results still take time and waiting for them will prolong patients' length of stay in ED and thus risk overburdening health care provision. The HOME-CoV study was designed as a pragmatic

trial dealing with the real issues at hand when deciding between outpatient care or hospitalization. This reinforces the applicability of our results.

During the interventional period, in the adjusted population, more than half of the patients had a negative HOME-CoV rule and the emergency physician in charge complied with the rule in 90%. As a result, 45% of the patients had a negative rule and were discharged home after ED assessment. None of them had an adverse outcome. However, our study failed to show a significant increase in the rate of patients managed at home with the implementation of the HOME-CoV rule, a third of patients being hospitalized during each period, a rate in line with recent publications: 32% in a large cohort in New York City and 28% in the Danish nationwide cohort [19,20]. Indeed, the increase in the rate of patients with a negative rule who were managed at home was balanced out by a decrease in the rate of patients with a positive rule who were discharged to their homes. This result suggests that physicians, in their decision-making, take individual patient risk assessment into account to a greater extent when they applied the HOME-CoV rule than when they used their gestalt. However, it also suggests an overuse of the HOME-CoV rule. Indeed, the HOME-CoV rule was intended to define criteria for home treatment (if negative) rather than criteria for hospitalization (if positive). Our trial confirms that patients with a negative rule had a very low risk of adverse outcome and could be safely treated at home, but it also shows that some patients with a positive rule could be treated at home with a low risk of adverse outcome too. This result could be explained by the organization of a close ambulatory follow-up of patients with probable or confirmed COVID-19 in many hospitals, in order to increase home treatment. Another explanation could be the impact of the local caseload in the ED and in the hospital. Due to the before/after design of our study, a lower hospital caseload during the interventional period is likely and may have influenced the rate of hospitalization of patients with a positive HOME-CoV rule. Indeed, a qualitative study of decision-making amongst emergency physicians shows that the extent to which the ED is busy has an influence on decisions to increase patient admission [21].

The rate of adverse outcome defined as invasive ventilation or death was low as compared to previous studies and significantly lower during the interventional period than the observational period. This could be related to a decrease over time in the use of intubation for the benefit of non-invasive

ventilation of COVID-19 patients [22]. However, a similar trend was observed when we considered hospitalization with oxygen therapy or all-cause mortality as a judgement criterion. It is notable that the difference in adverse outcome was observed only in hospitalized patients, for which the most likely explanation is a multifactorial improvement of care including corticoid and antiviral therapy, thromboprophylaxis, and respiratory failure management [23].

The strength of our trial is its large panel of participating centers and patients and its prospective and pragmatic design. This reinforces the generalizability and applicability of our results. We included patients with confirmed or probable COVID-19, thus corresponding to the actual daily ED population that may benefit from the implementation of the HOME-CoV rule as a tool in decision-making [24]. Moreover, the same results were observed in the overall population and in the subgroup of patients with a positive RT-PCR for SARS-CoV2, reinforcing their validity. Finally, the HOME-CoV rule is exclusively based on clinical criteria that are easy to assess, even by phone, and may be a helpful tool not only for all frontline and emergency physicians but also for general practitioners, geriatricians, and infectious disease consultants.

Our study has some limitations. Firstly, we used a quasi-experimental before-and-after design by taking into account resource constraints (the Emergency Departments faced with the pandemic) and time constraints (the need to provide prospective validation of the HOME-Cov rule and practice guidelines as soon as possible). Our results should optimally be confirmed in a formal cluster randomized trial. Secondly, the rate of patients who had an unfavorable outcome and required invasive ventilation or who died was lower than expected at the time we designed the trial. Indeed, recent data have demonstrated mortality rates lower than those observed in the early phases of the epidemic in Wuhan [14,25]. Furthermore, and in contrast to previous studies, patients presenting severe cases of the disease at admission and requiring immediate intensive care were excluded. Indeed, the severity of these patients' symptoms was such that home treatment was not even an option.

INTERPRETATION

A negative HOME-CoV rule qualified more than 40% of ED patients with probable or confirmed COVID-19 for home treatment, with a very low risk of adverse outcome.

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Author Contributions: PMR and DD designed and supervised the study. PA, MF, CA, GS, ST, ME, TPC, GA, DAD, BK, BP, VM, JLM, SC, SD supervised the study in their respective centres and included a large number of patients. DD and JR performed statistical analysis. DD and PMR drafted the manuscript and all authors contributed substantially to its revision. DD and PMR takes responsibility for the paper as a whole.

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Take Home Point:

Study question: Is the HOME-CoV rule reliable for identifying a subgroup of COVID-19 patients with a low risk of adverse outcomes who can be safely treated at home?

Results: Among patients with a negative HOME-CoV rule who represented 41% (1239/3000) of patients presenting to the Emergency Department with probable or confirmed COVID-19, 0.32% (4/1239) had an adverse outcome (invasive ventilation or death) within the following 7 days, the overall rate of complications being lower afterwards versus before the implementation of the rule but without significant difference in the rate of home treatment.

Interpretation: A large proportion of ED patients with probable or confirmed COVID-19 have a negative HOME-CoV rule and can be safely treated at home with a very low risk of complication.

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Legends

Tables

Table 1. HOME-CoV rule

Table 2. Baseline and adjusted characteristics of the patients in the observational and interventional period.

Table 3. Clinical evolution at 7 days according to the HOME-CoV Rule and performance of the performances of the HOME-CoV rule (cut-off ≥ 1).

Table 4. Comparison of the rate of evolution toward severe COVID-19 according to the HOME-CoV rule and according to patient management (adjusted population).

Figures

Figure 1. Flowchart.

Figure 2: Classification of patients according to the two periods and to the Ordinal Scale of Clinical Improvement of COVID-19 at inclusion, Day 7 and Day 28.

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

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

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Patient characteristics	Prior weighting-based Propensity score		After weighting-based Propensity score	
	Observational period n=1763	Interventional period n=1370	Observational period n=1274	Interventional period n=1274
Demographic characteristics				
Age – mean ± SD – yr	54.2 ± 19.8	52.3 ± 19.8	52.9 (19.7)	52.6 (19.9)
Female sex – no. (%)	952 (54)	757 (55.3)	704 (55.3)	705 (55.3)
Medical history – no. (%)				
Severe cognitive impairment	18 (1.0)	6 (0.4)	10 (0.8)	7 (0.5)
COPD stage III/IV	33 (1.9)	23 (1.7)	22 (1.7)	22 (1.7)
Chronic respiratory failure	27 (1.5)	18 (1.3)	18 (1.4)	17 (1.3)
Controlled or unstable asthma	181 (10.3)	151 (11)	148 (11.6)	140 (10.9)
Severe or end-stage renal disease (GFR < 30ml/min)	38 (2.2)	18 (1.3)	18 (1.4)	17 (1.3)
Hepatic cirrhosis child B or child C	10 (0.6)	7 (0.5)	7 (0.5)	6 (0.5)
Chronic cardiac failure NYHA III/IV	24 (1.4)	13 (0.9)	14 (1.1)	13 (1.0)
Hypertension	530 (30.1)	361 (26.4)	345 (27.1)	343 (26.9)
Diabetes	226 (12.8)	145 (10.6)	136 (10.7)	133 (10.4)
History of thromboembolism	96 (5.4)	71 (5.2)	65 (5.1)	66 (5.2)
Cancer history or active cancer	162 (9.2)	117 (8.5)	118 (9.3)	112 (8.8)
Immune deficiency and HIV	56 (3.2)	35 (2.6)	32 (2.5)	32 (2.5)
Inadequate living conditions	272 (15.4)	142 (10.4)	140 (11.0)	139 (10.9)
Signs and symptoms – no. (%)				
Anosmia, ageusia, dysgeusia	511 (29)	312 (22.8)	291 (22.8)	244 (19.2)
Cough	1175 (66.6)	837 (61.1)	763 (59.9)	770 (60.4)
Dyspnea	1147 (65)	815 (59.5)	753 (59.1)	737 (57.8)
Diarrhea	481 (27.3)	385 (28.1)	320 (25.1)	346 (27.1)
Chest pain	635 (36.0)	513 (37.4)	463 (36.3)	462 (36.3)
Confusion, impaired alertness	92 (5.2)	44 (3.2)	43 (3.4)	43 (3.4)
Worsening in the last 24 hours	869 (49.3)	540 (39.4)	500 (39.2)	498 (39.1)
Heart rate ≥ 120 beats/min	90 (5.1)	100 (7.3)	92 (7.2)	94 (7.4)
Systolic blood pressure < 90mmHg	12 (0.7)	8 (0.6)	9 (0.7)	10 (0.8)
Temperature, mean ± SD, °C	37.03 ± 1.0	36.8 ± 1.0	36.9 ± 0.9	39.9 ± 1.0
Body mass index ≥30kg/m^2	230 (13.0)	203 (14.8)	205 (16.1)	206 (16.2)
Pulse oxygen saturation ≤94% in ambient air or necessity of oxygen therapy	399 (22.6)	259 (18.9)	268 (21.0)	272 (21.4)
Respiratory rate ≥25/min	310 (17.6)	192 (14)	197 (15.5)	198 (15.5)
Ability to speak or count without resuming breathing < 8 seconds	209 (11.9)	99 (7.2)	103 (8.1)	105 (8.2)

Table 3. Clinical evolution at 7 days according to the HOME-CoV Rule and performance of the performances of the HOME-CoV rule (cut-off ≥ 1).

	Total n= 3000	Patients with adverse evolution, n=57	Patients without adverse evolution, n= 2943
HOME-CoV rule positive	1761	53	1708
HOME-CoV rule negative	1239	4	1235

Sensibility: 0.93 (95%CI 0.84 to 0.98)
Specificity: 0.42 (95%CI 0.40 to 0.44)
Negative predictive value: 0.996 (95%CI 0.98 to 1.00)
Positive predictive value: 0.29 (95%CI 0.13 to 0.35)
Negative likelihood ratio: 0.16 (95%CI 0.06 to 0.42)
Positive likelihood ratio: 3.03 (95%CI 2.56 to 3.58)

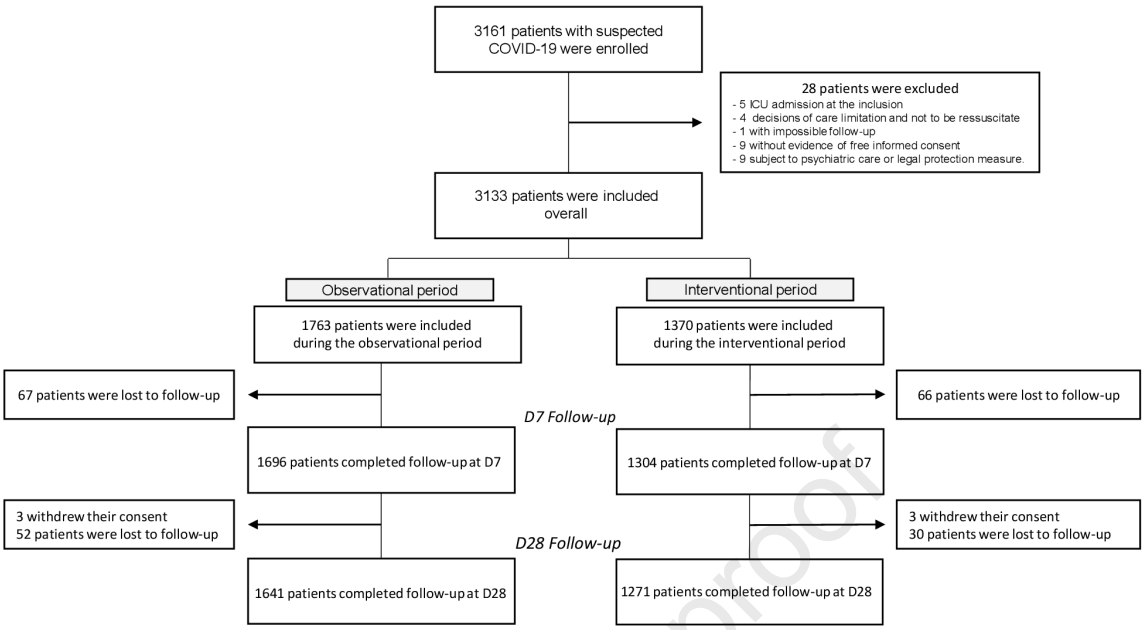
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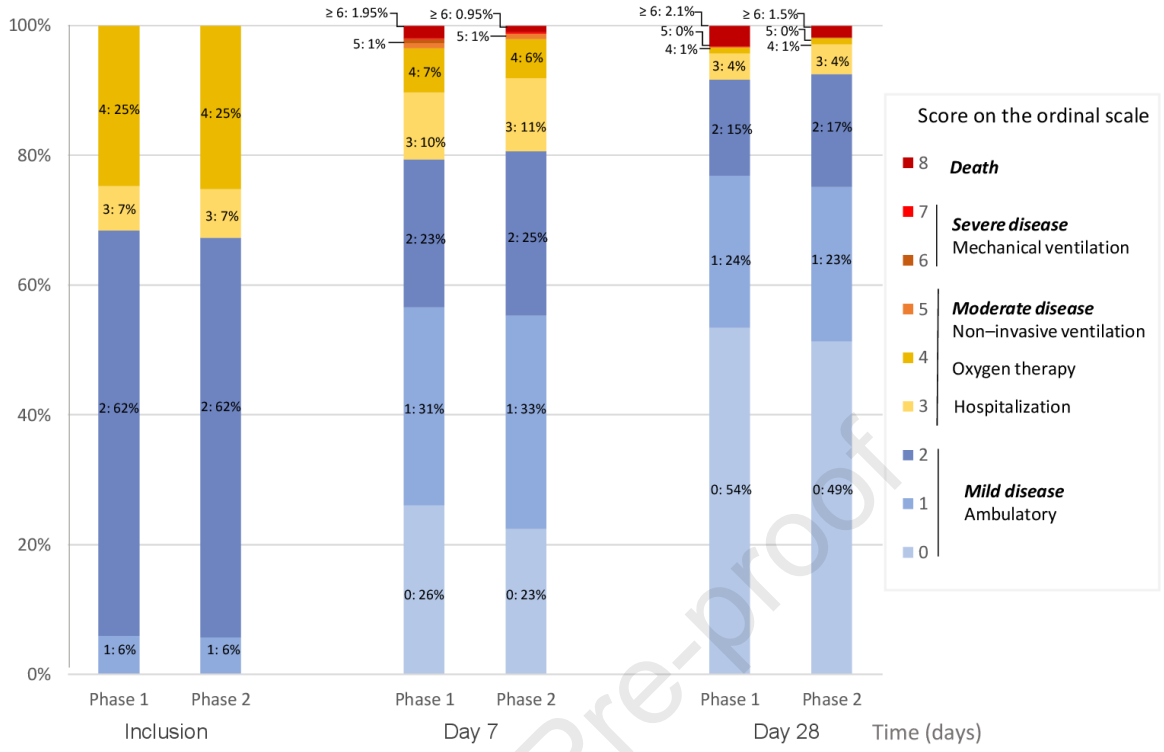
		Observational period		Interventional period		Comparison
Patient management						
HOME-CoV Rule	*Management*	N patients	%	N patients	%	Absolute difference (95%CI)
Positive	Home treatment	374/1243	30.1	296/1235	24	- 6.1% (-9.5 to -2.6)
	Hospitalization	320/1243	25.7	312/1235	25.26	- 0.4% (-3.9 to 3.0)
Negative	Home treatment	474/1243	38.1	560/1235	45.3	+ 7.2% (3.3 to 11.1)
	Hospitalization	75/1243	6.0	67/1235	5.4	- 0.6% (-1.2 to 2.5)
Evolution toward a severe COVID-19						
HOME-CoV Rule	*Management*	N patients	%	N patients	%	Absolute difference (95%CI)
Positive	Home treatment	1/374	0.3	1/296	0.3	0
	Hospitalization	31/320	9.8	17/312	5.4	- 4.4% (-5.7 to -2.4)
Negative	Home treatment	0/474	0	0/560	0	0
	Hospitalization	3/75	3.4	1/67	1.5	- 1.9% (-3.2 to -0.8)

*Severe COVID-19 was defined as cases in which patients were either undergoing mechanical ventilation or dead.
95%CI: 95% confidence interval

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Abbreviations List

AUC: Area Under the Curve

COVID-19: Coronavirus Disease 2019

ED: Emergency Department

HOME-CoV: Hospitalization or Outpatient ManagEment of patients with SARS-CoV-2 infection

RT-PCR : Reverse Transcriptase-Polymerase Chain Reaction

WHO-OSCI: World Health Organization - Ordinal Scale for Clinical

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