Senior-COVID-Rea Cohort Study: A Geriatric Prediction Model of 30-day Mortality in Patients Aged over 60 Years in ICU for Severe COVID-19

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**Supplementary Table 1. STROBE Statement.** Checklist of items that should be included in reports of observational studies.

| Item No. | Recommendation | Page No. | Relevant text from manuscript |
|----------|----------------|----------|-------------------------------|
| 1        | (a) Indicate the study’s design with a commonly used term in the title or the abstract | 1        | multicentre observational cohort study |
|          | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 4-5      |                                       |
| 2        | Explain the scientific background and rationale for the investigation being reported | 7        | According to recent evidence from two studies, disease outcomes of COVID-19 patients admitted to hospital would be better predicted by frailty than either age or comorbidity. |
| 3        | State specific objectives, including any prespecified hypotheses | 8        | we conducted a multicentre observational study to determine the clinical and biological covariates predictive of mortality in the population of patients over 60 years of age admitted in intensive care unit, with a specific attention paid to a retrospective and declarative assessment of their geriatric parameters 1 month before COVID-19 infection. This first analysis explores the respective impacts of various geriatric parameters and discusses their respective properties. |
| 4        | Present key elements of study design early in the paper | 9        | Senior-COVID-Rea study is a multicenter observational cohort study |
| 5        | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 9        | Data were collected across seven ICUs in Auvergne Rhone Alpes Region, France. A standardised case report format was used for recording data collected. |
| 6        | (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  
Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  
Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants | 9        | All patients aged 60 or older admitted to the participating ICUs with a diagnosis of COVID-19 were screened and included provided their (or their relative’s) agreement. Diagnostic criteria were laboratory-confirmed SARS-CoV-2-positive swabs or a radiological diagnosis made by lung CT-scan consistent with COVID-19. Patients were excluded during data analysis only when duplicates were found, due to patients transferred from one ICU to the other from the participating centres. No other exclusion criteria were applied. |
## SUPPLEMENTARY DATA

### (b) Cohort study

For matched studies, give matching criteria and number of exposed and unexposed cases.

| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. |
|-----------|---|----------------------------------------------------------------------------------------------------------------------------------|
| Data sources/measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. |
| Bias | 9 | Describe any efforts to address potential sources of bias. |
| Study size | 10 | Explain how the study size was arrived at. |

In this analysis, only primary outcome was analysed, i.e., the day-30 mortality (time from ICU admission).

The first hypothesis of Senior-COVID-Rea was based on the first results of first Chinese retrospective results (1): considering a single analysis variable (age), with expected mortality of 30% in patients under 70 years of age, and 70% in patients over 70 years of age (with 40% of patients over 70 years of age), a total of 130 patients was expected to show a statistically significant difference between these two groups with a power of 90% (bilateral alpha risk test of 5%). Since the analysis considered the integration of several factors, considering 15 factors, hoping for a coefficient of determination of 0.5 of the model, to achieve an optimism of less than

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10%, 185 patients were to be included (criterion 1 of Riley, Snell et al, (15)).

After the publication of data on mortality in ICU in Lombardy region, Italy in April 2020 (2), considering that a stopping of the trial at 185 patients would impair its statistical power and induce a potential risk of patients’ selection bias, the scientific committee decided, on the 7th May, that all the patients admitted to ICU before that date - that corresponded to the end of the first COVID wave – should be screened and proposed the study without any patients’ number limitation.

This sample size calculation was modified on Clinicaltrials.gov site accordingly (July 28, 2020).

Quantitative variables 11

| Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
|---|
| Continuous variables were described by the mean, standard deviation (SD), and range. Categorized variables were described by the frequency and percentage of each modality. Common thresholds were applied: CFS ≥5, ADL <6, IADL8 <8, Fried score >2. |

Statistical methods 12

| (a) Describe all statistical methods, including those used to control for confounding |
|---|
| The effect of factors on day-30 mortality risk was quantified by odds ratios (with their associated 95% Confidence Interval, 95% CI). Factors with a p-value less than 0.20 in univariate were included in the multivariate analyses (logistic regression) |

| (b) Describe any methods used to examine subgroups and interactions |
|---|
| The overlap between the different categorized factors was analyzed through a Venn diagram. During the multivariate analyses, the collinearity between factors was analyzed through variance inflation factors (VIF); with a threshold above 1.5. |

| (c) Explain how missing data were addressed |
|---|
| No imputation of missing variables was performed |

| (d) Cohort study—If applicable, explain how loss to follow-up was addressed |
|---|
| Case-control study—If applicable, explain how matching of cases and controls was addressed |
| Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy |

| (e) Describe any sensitivity analyses |
|---|
| Subgroup analyses are not relevant in this study, but a cross-validation analysis was performed to assess the optimism of the model. |

Results

| Participants 13* |
|---|
| (a) Report numbers of individuals at each stage of study—e.g numbers potentially eligible, examined for eligibility, confirmed eligible, |
| STROBE flow diagram (Figure 1) |

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included in the study, completing follow-up, and analysed

(b) Give reasons for non-participation at each stage 11 STROBE flow diagram (Figure 1)

(c) Consider use of a flow diagram 11 STROBE flow diagram (Figure 1)

| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders 11 Table 1 |
|------------------|-----|-----------------------------------------------------------------------------------------------------------------------------------------|
|                  |     | (b) Indicate number of participants with missing data for each variable of interest 11 Table 1 |
|                  |     | (c) Cohort study—Summarise follow-up time (eg, average and total amount) na Short time endpoint (30 days), no missing data |

| Outcome data    | 15* | Cohort study—Report numbers of outcome events or summary measures over time 11 Table 2 |
|-----------------|-----|--------------------------------------------------------------------------------------------|
|                 |     | Case-control study—Report numbers in each exposure category, or summary measures of exposure |
|                 |     | Cross-sectional study—Report numbers of outcome events or summary measures |

| Main results    | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included 11 Table 3 |
|-----------------|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                 |     | (b) Report category boundaries when continuous variables were categorized 11 Table 3 |
|                 |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period na |

| Other analyses  | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses 10, 12 The overlap between the different factors was analyzed through a Venn diagram, using the categorized version of the different factors. Moreover, during the multivariate analyses, the collinearity between factors was analyzed through variance inflation factors (VIF). Table 4 |

| Discussion      | 18  | Summarise key results with reference to study objectives 12 Our results confirm our primary hypothesis, patients over 75 having, in this study, an almost 5-fold higher risk of D30 mortality, compared to younger ones (OR 4.82 (95%CI, 2.56-9.06), p<0.001). More precisely, D30 death rates varied from 15% in patients aged |

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### Limitations

| 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 14 | due to the study structure evaluating patients admitted to ICU, frail patients were poorly represented in the cohort, impairing de facto discrimination properties of frailty scores. |

### Interpretation

| 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 15 | When considering functional impairment, one may be surprised since impairment in IADL appears more discriminative than impairment in ADL, as ADLs are usually considered as laterly affected in the spectrum of dependence. Moreover, in their recently published model, Bousquet et al identified impairment in ADL but not in IADL as significantly associated with D30 mortality in an older COVID-19 population admitted in geriatric wards (26). One response may be linked to a low statistical power, since IADL impairment concerned 33% of the population when ADL impairment affected “only” 20% of the population, ADL impaired patients being frequently considered as unfit for resuscitation. |

### Generalisability

| 21 | Discuss the generalisability (external validity) of the study results | 16 | To conclude, age and IADL provide independent prognostic factors for D30 mortality in patients over 60 admitted in ICU for severe COVID-19 infection. Our triage model may be considered as useful to integrate into the individualized resuscitation proposal whereas exponential increase in COVID-19 incidence induces increasing constraints on healthcare systems. A future study is about to be launched, to externally validate the model. |

### Other information

#### Funding

| 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 16 | All the authors declare a grant from Hospices Civils de Lyon, during the conduct of the study, for Clinical Research Assistants and statistical analysis, no other competing interests with the considered topic. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
### Supplementary Table 2. TRIPOD checklist.

| Section/Topic | Item | Checklist Item | Page |
|---------------|------|----------------|------|
| **Title and abstract** | | | |
| Title | 1 | Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted. | 1 |
| Abstract | 2 | Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions. | 4 |
| **Introduction** | | | |
| Background and objectives | 3a | Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models. | 7-8 |
| | 3b | Specify the objectives, including whether the study describes the development or validation of the model or both. | 8 |
| **Methods** | | | |
| Source of data | 4a | Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable. | 9-10 |
| | 4b | Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up. | 11 |
| | 5a | Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres. | 9, 17 |
| Participants | 5b | Describe eligibility criteria for participants. | 9 |
| | 5c | Give details of treatments received, if relevant. | na |
| Outcome | 6a | Clearly define the outcome that is predicted by the prediction model, including how and when assessed. | |
| | 6b | Report any actions to blind assessment of the outcome to be predicted. | na |
| Predictors | 7a | Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured. | 10 |
| | 7b | Report any actions to blind assessment of predictors for the outcome and other predictors. | na |
| Sample size | 8 | Explain how the study size was arrived at. | 10 |
| Missing data | 9 | Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method. | 11 |
| | 10a | Describe how predictors were handled in the analyses. | 10, 11 |
| Statistical analysis methods | 10b | Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation. | 10, 11 |
| | 10d | Specify all measures used to assess model performance and, if relevant, to compare multiple models. | 10, 11 |
| Risk groups | 11 | Provide details on how risk groups were created, if done. | 10 |
| Results | | | |
| Participants | 13a | Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful. | 11 (Figure 1) |
| | 13b | Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome. | 11 (Table 1) |
Supplementary Table 3. Risk factors of day-30 mortality: multivariate analyses (continuous variables).

| Variables | Model 1 (step 1) |   | Model 2 (step 2) |   | Model 3 (step 3) |   |
|-----------|------------------|---|------------------|---|------------------|---|
|           | OR [95% CI]      |   | VIF              |   | OR [95% CI]      |   |
| Age (per 10 years increase) | 3.41 [1.99, 6.11] | <0.001 | 1.08 | Age (per 10 years increase) | 2.96 [1.79, 5.09] | <0.001 | 1.03 |
| Nb of grade≥2 CIRS-G comorb. | 1.10 [0.89, 1.36] | 0.395 | 1.19 | Nb of grade≥2 CIRS-G comorb. | 1.10 [0.09, 1.35] | 0.356 | 1.14 |
| ADL | 1.12 [0.58, 2.31] | 0.747 | 2.56 | ADL | 1.28 [0.69, 2.57] | 0.451 | 2.35 |
| IADL8 | 0.81 [0.63, 1.05] | 0.113 | 3.19 | IADL8 | 0.76 [0.62, 0.94] | 0.011 | 2.20 |
| Fried score | 1.15 [0.85, 1.57] | 0.362 | 1.63 | Fried score | 1.12 [0.83, 1.50] | 0.454 | 1.56 |
| CPS | 1.02 [0.69, 1.53] | 0.908 | 3.33 | Fall in last 6 mo. | 1.36 [0.49, 3.69] | 0.553 | 1.26 |
| Fall in last 6 mo. | 1.38 [0.49, 3.78] | 0.531 | 1.26 | |
| Model 4 (step 4) | | | Model 5 (step 5) | | Model 6 (Final) | |
| Age (per 10 years increase) | 3.04 [1.84, 5.22] | <0.001 | 1.02 | Age (per 10 years increase) | 3.11 [1.89, 5.33] | <0.001 | 1.01 |
| Nb of grade≥2 CIRS-G comorb. | 1.11 [0.91, 1.36] | 0.311 | 1.14 | Nb of grade≥2 CIRS-G comorb. | 1.13 [0.93, 1.38] | 0.223 | 1.08 |
| IADL8 | 0.79 [0.68, 0.93] | 0.005 | 1.32 | IADL8 | 0.77 [0.67, 0.89] | <0.001 | 1.07 |
| Fried score | 1.11 [0.84, 1.46] | 0.458 | 1.37 | |

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Supplementary Figure 1. STROBE Flow diagram

Hospitalized patients over 60 in COVID-19 units (screened: 290; duplicates: 3; n=287)

Not included (n= 56)
- Not meeting inclusion criteria (n=0)
- Declined consent (n=16)
- Other reasons (lack of time availability, n=40)

Recruited in the study (n= 231)
- Positive COVID-19 PCR (n= 209)
- CT-scan (n= 22)

Geriatric functional data (1 month before)

Analysed for primary endpoint (D30 mortality) (n= 231)
Supplementary Figure 2. Venn diagram displaying extent of overlap of geriatric vulnerability parameters in Senior-COVID-Rea population (n=231). ADL: patients with ≥1 impaired activity of daily living (n=45); CFS≥5 (n=24); CIRS-G: patients with 3 or more grade≥2 CIRS-G comorbidities (n=79); IADL: patients with ≥1 impaired activity of daily living according IADL8 score (n=74).