Identification and Validation of Clinical Phenotypes with Prognostic Implications in Hospitalized COVID-19 Patients. A multicentre cohort-based study.

Authors: Belén Gutiérrez-Gutiérrez, PhD;[1,2,3] María Dolores del Toro, PhD; [1,2,3] Alberto Borobia, PhD;[4,5] Antonio Carcas, PhD;[4, 5] Inmaculada Jarrín, Msc;[6] María Yllescas, PharmD;[7] Pablo Ryan, PhD;[8] Jerónimo Pachón, PhD;[2,3 9] Jordi Carratalà, PhD; [10,11,12] Juan Berenguer, PhD;[13,14] Jose Ramón Arribas; MD;[5,15] Jesús Rodríguez-Baño, PhD; [1,2,3] the REIPI-SEIMC COVID-19 and COVID@HULP groups.*

*Other members of the REIPI-SEIMC COVID-19 and COVID@HULP groups are listed in appendix pp 19–30.

Affiliations:

[1]Unidad Clínica de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Hospital Universitario Virgen Macarena, Sevilla, Spain

[2]Departamento de Medicina, Universidad de Sevilla, Sevilla, Spain

[3]Instituto de Biomedicina de Sevilla (IBiS), Sevilla, Spain.

[4]Departamento de Farmacología Clínica, Hospital Universitario La Paz, Universidad Autónoma de Madrid, Madrid, Spain.

[5]Instituto de Investigación La Paz (idiPAZ), Madrid, Spain.

[6]Centro Nacional de Epidemiología, Instituto de Salud Carlos III, Madrid, Spain.

[7]Fundación SEIMC/GeSIDA, Madrid, Spain.

[8]Servicio de Medicina Interna, Hospital Universitario Infanta Leonor, Madrid, Spain.

[9]Unidad Clínica de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Hospital Universitario Virgen del Rocío, Sevilla, Spain.

[10]Servei de Malalties Infeccioses, Hospital Universitari de Bellvitge, Barcelona, Spain

[11]Instituto de Investigación Biomédica de Bellvitge (IDIBELL), Barcelona, Spain

[12]Universitat de Barcelona, Barcelona, Spain.

[13]Servicio de Microbiología Clínica y Enfermedades Infecciosas, Hospital General Universitario Gregorio Marañón, Madrid, Spain.

[14]Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain.

[15]Unidad de Enfermedades Infecciosas, Servicio de Medicina Interna, Hospital Universitario La Paz, Madrid, Spain.

Corresponding author:

Jesús Rodríguez-Baño, Servicio de Enfermedades Infecciosas, Hospital Universitario Virgen Macarena, Avda Dr Fedriani 3, 41009 Seville, Spain

Email: jesusrb@us.es. Phone number: +34 661437062

Key words: COVID-19, SARS-CoV-2, viral infection, phenotypes, mortality, clinical features

This study was presented at the ESCMID Conference on Coronavirus Disease (ECCVID), 23-25 September 2020.

SUMMARY

Background. Clinical presentation of COVID-19 in admitted patients is heterogeneous. We aimed to determine whether clinical phenotypes of patients with COVID-19 can be derived from clinical data; to assess their reproducibility and correlation with prognosis; and to derive and validate a simplified probabilistic model for phenotypes assignment. Phenotypes identification was not primarily intended as a predictive tool for mortality.

Methods. Retrospective analysis of data from cohorts of hospitalised patients with COVID-19. Phenotypes were derived and reproduced in two randomly selected subsets of a multicentre cohort including 4,035 patients from 127 hospitals in Spain (a derivation [DC] and an internal validation cohort [IVC]) using a two-step cluster analysis of 72 clinical, laboratory and radiographic variables. A probabilistic model for phenotypes assignment was derived in the DC using multinomial logistic regression and validated in the IVC; it was also applied to an external validation cohort (EVC) including 2,226 patients. The 30-day mortality and other prognostic variables were assessed in the derived phenotypes and in the phenotypes assigned by the probabilistic model.

Findings. Three distinct phenotypes were derived in the DV and reproduced in the IVC: phenotype A (19·3% and 17·0% of patients in the DV and IVC, respectively) included younger patients, less frequently males, with mild "viral" symptoms and absence of inflammatory parameters; phenotype B (73·3% and 74·5%) included more obese patients, with lymphocytopenia, and moderately elevated inflammatory parameters; and phenotype C (7·3% and 8·5%) included older patients, with more comorbidities and even higher inflammatory parameters. A simplified probabilistic model (validated in the IVC) for phenotypes assignment including 16 variables was developed. 30-day mortality rates were 2·5%, 30·5% and 60·7% among patients with phenotypes A, B and C, respectively,

in the DC (log rank test, p<0·0001); the predicted phenotypes in the ICV and EVC showed similar mortality rates of in the assigned phenotypes.

Interpretation. Hospitalised patients with COVID-19 can be classified into three phenotypes which correlate with (although not intended to be predictive of) mortality. A simplified tool for the probabilistic assignment of patients into phenotypes was developed and validated. These results might help to better classify patients for clinical management; the pathophysiological substrate of the phenotypes must be investigated.

Funding. Instituto de Salud Carlos III, Spanish Ministry of Science and Innovation (COV20/01031), and Fundación SEIMC/GeSIDA

RESEARCH IN CONTEXT

Evidence before this study

We searched PubMed, Scopus and medRxiv from January 9 to September 30, 2020, using the terms ["COVID-19" OR "SARS-CoV-2"] AND ["phenotypes" OR "clinical features"] with no language restrictions in order to detect any published study identifying and characterising phenotypes among COVID-19 patients. We found one study which identified 3 phenotypes in a cohort of 85 patients admitted to ICU, which were correlated with mortality, and one study as preprint in which phenotypes were studied in ambulatory patients using self-declaration of symptoms. Beyond that, we found studies referring to distress syndrome-associated phenotypes or to hyperinflammatory phenotypes. Therefore, to the best of our knowledge, this is the first study investigating the existence and characterisation of clinical phenotypes for COVID-19 patients at hospital admission.

Added value of this study

We identified three distinct clinical phenotypes based on demographics, underlying conditions, clinical and laboratory data, and radiologic features at presentation among patients hospitalised with COVID-19. The phenotypes were shown to have clinical implications since they are associated with the prognosis of patients; furthermore, we developed and validated a simplified probabilistic model for phenotypes assignment. This model is available as a tool at http://fen-covid.com/index.html to facilitate the probabilistic classification of admitted COVID-19 patients into phenotypes.

Implications of all available evidence

The identification of phenotypes opens the door to investigating potential differences in their underlying pathophysiological mechanisms, which would allow better pathogenesis-targeted approaches for therapies in the design and selection of participants in clinical

trials depending on the mechanism of action of specific drugs, and their use in clinical management. Also, phenotypes assignment would be helpful in identifying very low risk patients and patients who may need closer monitoring during admission.

INTRODUCTION

Patients hospitalized with COVID-19 show a wide variety of clinical signs and symptoms, and laboratory abnormalities; [1-5] some of these features have been found to be predictors of mortality.[3, 4]. The reasons for this heterogeneous presentation are not fully understood. However, they might be related to viral factors such as the viral load,[6] partial immune protection due to previous infections with other coronaviruses,[7] genetic determinants,[8] and other non-genetic mediated factors such as age and underlying conditions.[3, 4]

We hypothesize that patients hospitalized with COVID-19 might be classified into a limited number of clinical patterns (phenotypes) according to their demographics, underlying conditions, signs, symptoms, radiologic findings and laboratory data at presentation. If existing, these phenotypes might denote different pathophysiological routes and outcomes, and useful for better classifying the patients for testing treatment strategies.

The objectives of this study were to determine whether clinical phenotypes of patients with COVID-19 can be derived from clinical data; to assess their reproducibility and correlation with prognosis; and to derive and validate a simplified probabilistic model for phenotypes assignment.

METHODS

Databases

We used the data from two cohorts: the COVID-19@Spain cohort, a retrospective cohort including 4,035 consecutive hospitalized COVID-19 patients from 127 hospitals in Spain

from February 2nd until March 17th, 2020, and the COVID-19@HULP cohort, including 2,226 consecutive patients admitted to a teaching hospital in Madrid from February 25th until April 19th 2020. Both included consecutive adult patients admitted with COVID-19; the designs and patients´ features were previously reported in detail.[4, 5] Forty-one patients in the COVID-19@HULP cohort included in the COVID-19@Spain cohort were excluded from the COVID-19@HULP cohort for the current study (remaining patients in this cohort, 2,185). The COVID-19@Spain cohort was divided into a derivation cohort, including 2/3 randomly selected patients (n=2,667) and an internal validation cohort, including the remaining 1,368 patients. The COVID-19@HULP cohort was used as an external validation cohort. An overview of the analyses performed in the derivation and validation cohort is shown in appendix, p 21. The study was approved by the University Hospitals Virgen Macarena and Virgen del Rocío ethics committee which waived the need to obtain written informed consent due to the observational nature of the study. STROBE recommendations were followed (appendix pp 2–3).

Phenotypes derivation

Overall, 69 variables were considered to derive the clinical phenotypes. The variables were selected based on the available information about the features of admitted patients[1-3] and the early clinical experience gained at the participating sites; all were collected at hospital admission and included age, gender, ethnicity, comorbidities, drugs previously used for underlying diseases, COVID-19-related signs and symptoms at presentation, laboratory, and chest radiographic data. The full list of variables is shown in table 1. Because our objective was to explore the existence of phenotypes, we did not make any preselection of variables.

The proportion of missing data per variable in the COVID-19@Spain cohort is shown in appendix (pp 5-6); after discarding that data were missing completely at random by the

Little's MCAR test, missing data were completed by multiple imputation using the Markov chain Monte Carlo method.

The analyses to identify the phenotypes were first performed in the derivation cohort. We first assessed the distributions of values and missing data, and the correlation among the variables, using the chi-square test and Pearson's correlation coefficient for categorical and continuous variables. Highly correlated variables were excluded. A two-step cluster analysis was performed using both continuous and categorical variables, which provided the optimal number of clusters. We used silhouette analysis to assess the quality of the clusters derivation. A sensitivity analysis excluding variables with >50% missing data was performed.

The features of the patients in the phenotypes obtained were compared using chi-square and Kruskal-Wallis tests for categorical and continuous variables; the patterns of distribution of the variables in the different phenotypes were visualized using chord diagrams and heatmaps after grouping variables into comorbidities and system/organ-related data as explained in figures 1 and 2, and in the appendix (p 4). The two-step cluster analysis was also performed in the internal validation cohort to check the reproducibility of phenotypes identification.

Derivation and validation of a parsimonious probabilistic model for phenotypes

Because the number of variables used to derive the phenotypes was very high, assigning patients to phenotypes is neither intuitive nor applicable for clinical practice. Therefore, we developed a simplified probabilistic model to assign patients into the phenotypes. To do so, and since we identified three phenotypes, we performed a multinomial logistic regression analysis in the derivation cohort. First, the bivariate association of each

variable with the phenotypes was analysed using the chi-square and Kruskal-Wallis tests for categorical and continuous variables. Those with a p value <0·20 were included in a multinomial logistic regression model; the variance inflation factor value was used to detect the potential occurrence of collinearity. Also, interactions were tested. The variables were selected using a manual backward selection process. The predictive ability of the final model for observed data was checked by calculating the area under the receiver operating characteristic curves (AUROC) with 95% confidence intervals (CI) for the three phenotypes. We also tested the predictive ability of the model in 60 randomly chosen subcohorts with 80%, 60% or 40% the sample size of the derivation cohort.

The probabilistic model for phenotype assignment was used in two ways. First, it was applied to the internal validation cohorts to check its ability to predict the phenotypes obtained from this cohort. And second, it was also applied to both the internal and external validation cohorts so to obtain a probabilistic assignment of patients to the phenotypes (the model-derive formula used for the probabilities calculation are in the appendix, p 4); patients were assigned to the phenotype with a higher belonging probability according to the model-derived formula. Then, we checked the distribution of variables among the assigned phenotypes.

Prognostic assessment of the phenotypes

We compared the 30-day mortality of patients in the different phenotypes in the derivation cohort by Kaplan-Meier curves and log-rank tests, and calculated the hazard ratios (HR) with 95% CI; patients discharged before 30 days were censored on the last day they were contacted. We also collected data on complications occurring during admission (listed in appendix, p 6). These variables were also analysed in the validation cohorts, in which patients were assigned to the phenotype with the highest probability according to the probabilistic model-derived formula. Because any association of phenotypes with

mortality might be caused by a different distribution of a few strong independent prognostic variables in the phenotypes such as age and oxygen saturation,[4] we performed stratified analysis to check if any mortality association was maintained in all strata of these variables.

All analyses were performed with IBM SPSS Statistics 26, SPM 8·2 and R software.

Patient involvement

We discuss the objectives of the study, the design and results with several healthcare workers who suffered COVID-19.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had access to all the data. The corresponding author had final responsibility for the decision to submit for publication.

RESULTS

The features of the patients in the cohorts used for this study were previously reported in detail.[4, 5] The two-step cluster analysis of variables collected at hospital admission identified three clinical phenotypes in the derivation cohort: phenotype A (516 patients, 19·3%), phenotype B (1,955 patients, 73·3%) and phenotype C (196 patients, 7·3%). The silhouette score was 0·6, indicating good quality of clustering. Exclusion of variables with a high proportion of missing data did not cause evident changes. Overall, patients with phenotype A were younger (mean age, 55·2 years, vs 68·7 and 77·2 in phenotypes B and C, respectively), less frequently male (55·2% vs 62·6% and 68·9%), presented more frequently with headache (19·0% vs 9·3% and 7·1%), myalgia (29·1% vs 25·8%

and 13·3%) and chest pain (14·7% vs 10·5% and 10·7%), had higher lymphocyte count (mean cells/µL, 1439 cells vs 1094 and 1096) and lower levels of inflammatory parameters such as C reactive protein, interleukin-6, ferritin or lactic acid dehydrogenase. Patients in phenotype B were more frequently obese (13·8% vs 7·8% and 3·5% in phenotypes A and C), more frequently reported fever (82·9% vs 80·2 and 68·9) and cough (73·6% vs 67·8% and 63·3%), more frequently had pulmonary infiltrates in chest radiography (19·8% vs 46·7% and 25·0%), interstitial infiltrates (44·9% vs 25·0% and 40·8%), and higher levels of ferritin (mean values, 809·5 ng/mL vs 616·3 and 752·8) and creatine phosphokinase (mean values, 164·3 vs 150·8 and 141·4). Finally, patients in phenotype C more frequently had chronic heart disease (56·1% vs 13·2% and 22·9% in phenotypes A and B, respectively), hypertension (85·7% vs 31·2% and 52·7%), chronic lung disease (31·1% vs 7·8% and 19·5%), chronic kidney disease and diabetes mellitus (48·5% vs 10·3% and 22·5%), acute altered mental status (17·9% vs 5·2% and 12·3%), higher levels of neutrophils (mean cells/µL, 8539 vs 4112 and 4892), D-dimer (mean values, 1343 µg/L vs 715 and 986), procalcitonin (mean values, 0·70 vs 0·17 and 0·27), C reactive protein (mean values, 127 mg/L vs 47 and 88), creatinine (mean values, 2·76 vs 0·96 and 0·99), potassium (mean values, 4·5 mEq/L vs 4·0 and 4·0), and worse oxygenation parameters (the specific data are shown in appendix, pp 7-10, and represented in figures 1 and 2).

The two-step cluster analysis was repeated in the internal validation cohort; this analysis also selected three clusters, with a very similar distribution of patients as in the derivation cohort: phenotype A, 233 patients (17·0%); B, 1019 (74·5%); and C, 116 (8·5%). The silhouette score was also 0·6; the distribution of variables in the phenotypes was the same than in the derivation cohort with the only exceptions of proportion of liver cirrhosis and active solid malignancy (which were not significantly different in the derivation cohort

while in the internal validation cohort were more frequent in phenotype C than in A or B), haematologic malignancy (not different in the derivation cohort but less frequent in phenotype A in the internal validation cohort), and ferritin and creatine phosphokinase levels (which were higher in phenotype B in the derivation cohort and in phenotype C in the internal validation cohort); the specific data are in the appendix, pp 11–14, 22-23.

In order to develop a simplified manner to assign patients to a phenotype, a parsimonious probabilistic model for belonging to phenotypes was developed and validated. We first performed a bivariate analysis of the association of the different variables with phenotypes A vs. C and B vs. C in the derivation cohort; as specified above, a significant crude association with phenotype was found for a high number of variables (table 1). After a variables selection process, a final multinomial logistic regression model with 16 variables was developed, including age, gender, chronic lung disease, obesity, diastolic blood pressure, oxygen saturation (room air), white blood cell count, neutrophils, haematocrit, coagulation international normalised ratio, C reactive protein, glucose, creatinine, sodium, potassium and type of lung infiltrate on chest radiograph (Table 2). Therefore, a simplified probabilistic model for patients' assignment to phenotypes was derived. The AUROC (95% CI) of the model for the observed data in the derivation cohort showed very good predictive ability for the three phenotypes: 0·86 (0·85–0·88), 0·88 (0·86–0·89) and 0·99 (0·99–0·99) for patients in phenotypes A, B and C, respectively (appendix p 24). The predictive ability was similar in the smaller, randomly selected subcohorts (appendix p 15).

The capacity of the model to correctly assign patients to the phenotypes was validated in the internal validation cohort for the phenotypes directly derived from that cohort. Its ability to predict the observed phenotypes in the internal validation cohort was also high:

the AUROC were 0·86 (95% CI: 0·84–0·89) for phenotype A, 0·86 (95% CI: 0.84–0.88) for B, and 0.95 (0·93–0·98) for C.

The probabilistic model was then applied to the internal and external validation cohorts to obtain the individual probability for being assigned to a specific phenotype. The number of patients in the internal validation cohort assigned to phenotypes A, B and C according to their highest probability were 263 (19·2%), 1021 (74·6%) and 84 (6·1%), respectively; the figures for the external validation cohort were 323 (14·7%), 1757 (80·4%), and 105 (4·8%). In the internal validation cohort, the distribution of all variables in the three predicted phenotypes was similar to that in the derivation cohort (appendix pp 16–17). For the external validation cohort, not all variables collected in the derivation cohort were available; therefore, we checked the distribution of the variables included in the model, which was similar to that in the derivation cohort (appendix p 18).

In the derivation cohort, 30-day mortality (95% CI) rates were 2·5% (1·4-4·3), 30·5% (28·5-32·6) and 60·7% (53·7-67·2) among patients with phenotypes A, B and C, respectively (log rank test, p<0·0001; figure 3). In the internal validation cohort, the mortality in the reproduced phenotypes were 2·6% (1·0-5·6) for phenotype A, 31·0% (28·2-33·9) for phenotype B and 53·4% (44·4-62·2) for phenotype C; log rank test, p<0·0001 (appendix pp 13-14). Regarding the phenotypes assigned based on the probabilistic model, the mortality rates for phenotypes A, B and C were: in the internal validation cohort, 5·3% (3·4-8·1), 31·3% (28·5-34·2) and 59·5% (48·8-69·3), respectively (log rank test, p<0·0001; appendix p 17 and figure 3); and in the external validation cohort, 3·7% (2·0-6·4), 23·7% (21·8-25·7) and 51·4% (41·9-60·7), respectively (log rank test, p<0·0001; appendix p 18 and figure 3). All mortality data are summarised in the appendix, p 19.

The proportion of patients who needed ICU care or suffered transfusion-requiring anaemia, pleural effusion, acute kidney failure, heart failure, bacterial pneumonia, acute respiratory distress syndrome and cardiorespiratory arrest during admission were also significantly more frequent in phenotype C and less frequent in phenotype A; the differences were not significant for stroke, ischemic coronary event, liver failure or disseminated intravascular coagulation (appendix, pp 9-10). The results were similar in the internal validation cohort with the exception that liver failure was more frequent in phenotype B, and in the external validation cohort for the available variables (appendix pp 17-18).

In order to check if the association of the phenotypes with mortality was maintained after considering the different distribution of strong mortality predictors across the phenotypes such as age and oxygen saturation, a stratified analysis per strata of these variables was performed in the derivation cohort. In all strata, phenotypes were significantly associated with mortality (appendix, p 20).

DISCUSSION

We identified three phenotypes based on demographics, underlying conditions, clinical and laboratory data, and radiologic features at presentation among patients hospitalised with COVID-19. The phenotypes, despite not intended to be rules for predicting mortality, were shown to have clinical implications since they are associated with the prognosis of patients; furthermore, we developed a simplified probabilistic model potentially applicable to other cohorts.

Clinical presentation of COVID-19 is polymorphic. Clinical phenotypes have been described for patients with severe acute respiratory distress with potential implications

for respiratory support therapy.[9] Also, phenotypes based only on non-hospitalised patients' self-declaration of symptoms using an app is available as a preprint.[10] Clinical phenotypes have been identified in sepsis,[11] and an hyperinflammatory "phenotype" has been proposed in COVID-19 patients.[12, 13] However, we are not aware of other studies specifically investigating the existence of diverse clinical phenotypes for COVID-19 patients at hospital admission, with the exception of a study in which three phenotypes based on clinical and laboratory features were also identified using hierarchical clustering in 85 patients admitted at ICU, using a limited number of variables.[14]

The phenotypes found were strongly associated with the prognosis. Differently from outcome predictive scores-generating studies or those identifying outcome predictors, in which the independent predictive association of each variable with the outcome is assessed, what phenotypes provide is information about how the population can be classified according to clustering of variables, and how such clusters are associated with the outcome. Because age and oxygen saturation are the stronger independent predictors of mortality,[4] a stratified analysis according to strata of these variables was performed; the results suggest that the association of phenotypes with mortality is not only due to the different distribution of these variables in the phenotypes but that the phenotypes are consistently associated to different mortality risks. It should be noted that the phenotypes are not expected to provide accurate prediction for the prognosis, as done by predictive modelling, as the outcome rates in the phenotypes finally depend on the exact distribution of the stronger outcome predictors in each population to which the phenotypes are applied. In this sense, phenotypes are complementary to predictive scores. Beyond that, they might reflect different profiles of pathogen and host interactions, as a consequence of different infecting viral load, natural or acquired humoral and cellular immune response against SARS-CoV-2 and/or cell-receptor features and expression, in

association with some genetic background.[6–8] Because the databases used in this study only included phenotypic profiles and manifestations, we cannot provide information about underlying immunological or virological mechanisms. Future studies might reproduce the phenotypes and investigate their correlations with virological, immunological and genetic data.

We did not analyse the duration of disease at hospital admission because the start of symptoms can be difficult to assess in many patients, and may be confused with manifestations related to their chronic conditions; in our experience, this is particularly frequent in older patients with comorbidities. It has been hypothesized that the duration of symptoms would be relevant to differentiate the "viral" and the "inflammatory" phases of the disease,[13] but a clear cut-off in the number of days to differentiate the phases cannot be defined.

Classification of patients into phenotypes might be useful to design treatment strategies. On one side, very low risk patients (e.g., those with phenotype A who are younger than 60 or with oxygen saturation >95%) can be identified, who would need lower degrees of watchfulness and care and might be discharged for ambulatory follow-up; also, patients without initial criteria for being admitted to ICU but belonging to phenotype B or C would need to be closely monitored during admission. Also, because some aspects of the pathophysiology of the infection in patients with different phenotypes might be different, the therapeutic approach might need to be tailored. Because phenotype C is formed by patients with laboratory parameters suggestive of an hyperinflammatory state, they might be selected to investigate the efficacy of anti-inflammatory drugs. This would allow a more specific and efficient design of randomized trials. However, whether these phenotypes are useful for clinical purposes would need a better understanding of the underlying mechanisms and specific studies.

Because the phenotypes were identified using a high number of variables, it would be difficult to apply in the clinical arena in the absence of automated big data management. Therefore, we developed and validated a simplified probabilistic prediction model for phenotypes assignment. A publicly available calculator (available at http://fen-covid.com/index.html) and app have been developed to facilitate the probabilistic classification of admitted COVID-19 patients into phenotypes using the probabilistic model for phenotypes assignment.

Some limitations of this study are the high proportion of patients classified into phenotype B, reflecting the profile of the patients admitted during the first weeks of the epidemic in rather saturated hospitals, the exclusive participation of Spanish hospitals, and the high proportion of missing data in several variables. Hospital admission criteria might be different in other countries or in different moments of the pandemic; however, the cohorts used included patients with different severity. Some symptoms might not have been reported by the more severe patients. Strengths include the use of well-characterised cohorts, the inclusion of a high number of variables from different domains, and the validations performed.

In conclusion, hospitalised patients with COVID-19 can be classified into phenotypes which have prognostic implications. A simplified tool for the probabilistic classification of patients into phenotypes was developed. Further studies are needed to elucidate the underlying pathophysiologic mechanisms leading to a particular phenotype.

CONTRIBUTORS

Study conception and design: JR-B, BGG, MDdT, JP, JC, PR, IJ, MY, JRA, JB. Acquisition of data: all members of the REIPI-SEIMC COVID-19 and COVID@HULP

groups. Analyses and interpretation of data: JR-B, BGG, MdT, AB, AC, JP, JC, PR, IJ, MY, JRA, JB. Manuscript draft: JRB, BGG, MDdT. Manuscript critical revision: all members of the REIPI-SEIMC COVID-19 Group. Obtaining funds: JR-B, PR, JB, JRA. All authors had access to the data; BGG and JR-B verified all data.

DECLARATION OF INTERESTS

I Jarrin has received honoraria for participating in advisory board from Gilead Sciences and educational activities from ViiV. J Berenguer has received research grants from AbbVie, Gilead Sciences, Merck, and ViiV; and honoraria for being speaker or advisory board participation from AbbVie, Gilead Sciences, Janssen, Merck, and ViiV. Jose R Arribas received fees for participating in advisory board, being speaker and research grant support from Viiv, Janssen, Gilead, MSD, Teva, Alexa and Serono. P. Ryan has received research grants from Gilead Sciences and Merck; and honoraria for being speaker or advisory board participation from Gilead Sciences, AbbVie and ViiV. J Rodríguez-Baño, B Gutiérrez-Gutiérrez, MD del Toro, J Pachón, J Carratalá, Alberto Borobia and Antonio Carcas declare no competing interests.

ACKNOWLEDGMENTS

The study was funded by Instituto de Salud Carlos III, Spanish Ministry of Science and Innovation (COV20/01031), and Fundación SEIMC/GeSIDA. In addition, Jesús Rodríguez-Baño, Belén Gutiérrez-Gutiérrez, Juan Berenguer, Inmaculada Jarrín, Jordi Carratalá, Jerónimo Pachón, and José R Arribas received funding for research from Plan Nacional de I+D+i 2013-2016 and Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Ciencia, Innovación y

Universidades - co- financed by European Development Regional Fund “A way to achieve Europe”, Operative program Intelligent Growth 2014-2020 through the networks: Spanish Network for Research in Infectious Diseases (REIPI) [RD16/0016/0001 (JRB, BGG, MDdT), RD16/0016/0005 (JC), and RD16/0016/0009 (JP)] and Spanish AIDS Research Network (RIS) [RD16/0025/0017 (JB), RD16/0025/0018 (JRA), RD16/0025/00XX (IJ)]. The funders had no role in the design, collection of data, analysis or decision to publish.

We thank Alejandro González-Herrero for programming of the web tool and app.

DATA SHARING STATEMENT

Data collected for the study, including deidentified participant data and a data dictionary defining each field in the set, will be made available to other investigators upon request to the corresponding author, after approval of a proposal by the REIPI-SEIMC COVID-19 and COVID@HULP groups boards, with a signed data access agreement, beginning with publication.

REFERENCES

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020; **382**:1708–20.
2. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T. Davidson KW and the Northwell COVID-19 Research Consortium. Presenting characteristics,

comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York city area. *JAMA* 2020; **323**:2052–9.

3. Docherty AB, Harrison EM, Green CA, et al. Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020; **369**:m1985.
4. Berenguer J, Ryan P, Rodríguez-Baño J, et al. Characteristics and predictors of death among 4,035 consecutively hospitalized patients with COVID-19 in Spain. *Clin Microbiol Infect* 2020; **26**:1525-36.
5. Borobia AM, Carcas AJ, Arnalich F, et al. A cohort of patients with COVID-19 in a major teaching hospital in Europe. *J Clin Med* 2020; **9**:1733.
6. Magleby R, Westblade LF, Trzebucki A, et al. Impact of SARS-CoV-2 Viral Load on Risk of Intubation and Mortality Among Hospitalized Patients with Coronavirus Disease 2019. *Clin Infect Dis* 2020. Published 30th Jun 2020; doi: 10.1093/cid/ciaa851.
7. Mateus J, Grifoni A, Tarke A, et al. Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. *Science* 2020: eabd3871.
8. Ellinghaus D, Degenhardt F, Bujanda L, et al. Genomewide association study of severe Covid-19 with respiratory failure. *N Engl J Med* 2020; **383**:1522-34.
9. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med* 2020; **46**:1099–102.
10. Sudre CH, Lee KA, Lochlainn MN, et al. Symptom clusters in Covid19: A potential clinical prediction tool from the COVID Symptom study app. medRxiv preprint posted 16 June 2020. doi: https://doi.org/10.1101/2020.06.12.20129056.

11. Seymour CW, Kennedy JN, Wang S, et al. Derivation, validation, and potential treatment implications of novel clinical phenotypes for sepsis. *JAMA* 2019**;** **321**:2003–17.
12. Sinha P, Calfee CS, Cherian S, et al. Prevalence of phenotypes of acute respiratory distress syndrome in critically ill patients with COVID-19: a prospective observational study. *Lancet Respir Med* 2020; **8**:1209-18.
13. Manson JJ, Crooks C, Naja M, et al. COVID-19-associated hyperinflammation and escalation of patient care: a retrospective longitudinal cohort study. *Lancet Rheumatol* 2020; **2**: e594-e602.
14. Azoulay E, Zafrani L, Mirouse A, Lengliné E, Darmon M, Chevret S. Clinical phenotypes of critically ill COVID-19 patients. *Intensive Care Med* 2020; **46**:1651-1652.
15. Cao W, Li T. COVID-19: towards understanding of pathogenesis. *Cell Res*. 2020; **30**:367–9.

FIGURES LEGENDS.

Figure 1. Chord diagram for the distribution of groups of variables in the phenotypes in the derivation cohort. The variables are grouped in categories. The phenotypes are depicted in different colours. For each phenotype, if a variable mean (for continuous variables) or proportion (for categorical variables) is significantly different to the mean or proportion in the full derivation cohort, a ribbon connects the phenotype and the variable group; the width of the ribbons correlates with the number of variables that are significantly different from those in the derivation cohort for that phenotype.

Figure 2. Heatmap for the distribution of continuous variables in the phenotypes in the derivation cohort. A colour gradient is used to show differences in mean values in relation to the full derivation cohort, towards red for higher values and blue for lower values. The colour gradient indicates the number of standard deviations that the average value in the subcohort of interest is below or above the average value in the full cohort.

Figure 3. Probability of death until day 30 according to phenotypes in derivation cohort (3A), internal validation cohort (3B) and external validation cohort (3C). P value for log rank test was <0·001 in the three cohorts.

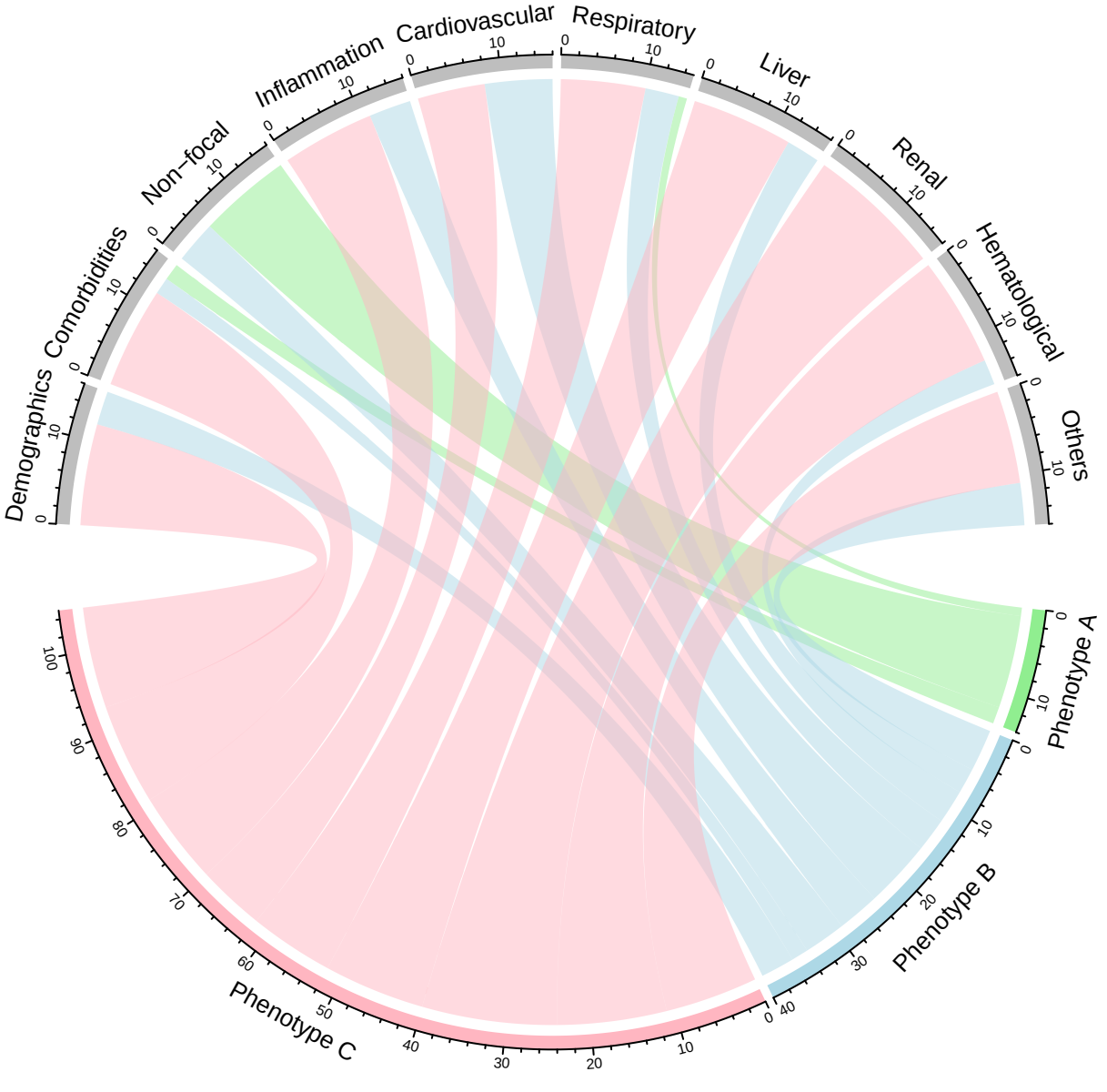
Table 1. Bivariate analysis of variables associated with phenotypes in the derivation cohort.

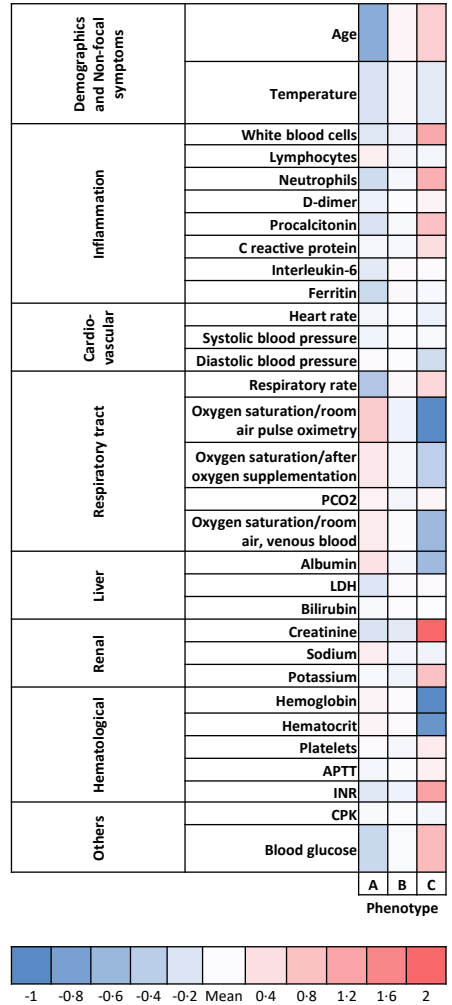
	Phenotype A vs Phenotype C[1]		Phenotype B vs Phenotype C[1]	
	Odds Ratio (95% CI)	**P value**	**Odds Ratio (95% CI)**	**P value**
DEMOGRAPHICS				
Age, per year	0·92 (0·90 –0·93)	<0·0001	0·96 (0·95–0·97)	<0·0001
Female gender	1·79 (1·27–2·54)	0·0014	1·32 (0·97–1·82)	0·089
Race				
Caucasian	0·48 (0·06–4·16)	0·50	0·48 (0·06–3·62)	0·48
African	0·80 (0·04–17·20)	0·89	0·10 (0·01–2·29)	0·15
Hispanic	2·08 (0·20–21·48)	0·54	1·08 (0·12–9·74)	0·94
Asian	0·20 (0·01–6·66)	0·37	0·55 (0·03–9·68)	0·68
Arab	0·50 (0·03–7·45)	0·61	0·40 (0·03–4·82)	0·47
Other	Reference		Reference	
COMORBIDITIES				
Chronic heart disease	0·12 (0·08–0·17)	<0·0001	0·23 (0·17–0·31)	<0·0001
Hypertension	0·08 (0·05–0·12)	<0·0001	0·19 (0·12–0·28)	<0·0001
Chronic lung disease	0·19 (0·12–0·29)	<0·0001	0·54 (0·39–0·74)	<0·0001
Asthma	1·75 (0·83–3·66)	0·14	1·73 (0·87–3·44)	0·12
Chronic kidney disease (stage)	0·05 (0·03–0·10)	<0·0001	0·06 (0·04–0·09)	<0·0001
Liver cirrhosis	0·76 (0·23–2·56)	0·65	0·75 (0·26–2·13)	0·59
Chronic neurological disease	0·45 (0·27–0·76)	0·0031	0·65 (0·43–1·00)	0·057
Active solid malignancy	0·63 (0·34–1·17)	0·14	0·73 (0·43–1·24)	0·21
Active haematological malignancy	0·83 (0·29–2·43)	0·74	0·90 (0·35–2·29)	0·82
HIV/AIDS	1·52 (0·17–14·29)	0·71	1·92 (0·26–14·29)	0·53
Obesity (BMI>30)	0·28 (0·18–0·45)	<0·0001	0·52 (0·37–0·74)	0·0043
Diabetes mellitus	0·12 (0·08–0·18)	<0·0001	0·31 (0·23–0·42)	<0·0001
Chronic inflammatory disease	1·33 (0·62–2·84)	0·47	1·20 (0·60–2·42)	0·60
Dementia	0·19 (0·10–0·35)	<0·0001	0·57 (0·38–0·87)	0·0086
Malnutrition	0·40 (0·21–0·76)	0·012	0·51 (0·31–0·86)	0·016
Smoking status				
Never	2·67 (1·88–3·81)	<0·0001	1·26 (0·93–1·71)	0·14
Yes	2·56 (1·37–4·79)	0·0037	1·11 (0·63–1·97)	0·71
Former smoker	Reference		Reference	
TREATMENTS FOR UNDERLYING CONDITIONS				
Angiotensin converting enzyme inhibitors	0·39 (0·25–0·59)	<0·0001	0·76 (0·54–1·08)	0·12
Angiotensin receptor blockers	0·41 (0·27–0·62)	<0·0001	0·57 (0·40–0·80)	0·0010
Inhaled corticosteroids	0·40 (0·24–0·67)	<0·0001	0·79 (0·53–1·19)	0·26
Systemic corticosteroids	0·61 (0·31–1·20)	0·15	0·69 (0·39–1·23)	0·22
Cancer chemotherapy	1·15 (0·41–3·23)	0·80	1·12 (0·45–2·86)	0·80
Biological drugs	1·08 (0·42–2·78)	0·87	0·65 (0·27–1·54)	0·32
INFECTION DATA AT ADMISSION				
NON–FOCAL SYMPTOMS				
Reported fever	1·85 (1·27–2·63)	0·0014	2·17 (1·59–3·03)	<0·0001
Temperature, per 1 degree Celsius	0·93 (0·78–1·11)	0·41	1·25 (1·06–1·46)	0·0063
Myalgia/arthralgia	2·70 (1·69–4·17)	<0·0001	2·27 (1·49–3·45)	<0·0001
Headache	3·03 (1·69–5·56)	<0·0001	1·33 (0·76–2·33)	0·32
Skin rash	0·95 (0·18–5·00)	0·95	1·10 (0·26–4·76)	0·89
Anosmia	3·51 (0·81–15·15)	0·098	1·77 (0·42–7·41)	0·44
Altered mental status	0·25 (0·15–0·43)	<0·0001	0·67 (0·45–0·99)	0·042
INFLAMMATION				
White blood cells, per 10^3 x cells/μL	0·79 (0·76–0·83)	<0·0001	0·83 (0·80–0·86)	<0·0001
Lymphocytes, per 10^3 x cell/μL	1·11 (0·97–1·28)	0·14	0·99 (0·86–1·14)	0·87
Neutrophils, per 10^3 x cells/μL	0·74 (0·70–0·78)	<0·0001	0·82 (0·79–0·85)	<0·0001
D–dimer, per 10^3 x μg/L	0·79 (0·66–0·93)	0·0050	0·98 (0·95–1·01)	0·18
Procalcitonin, per 1 x ng/mL	0·09 (0·04–0·17)	<0·0001	0·52 (0·44–0·61)	<0·0001
C reactive protein, per 10^2 x mg/L	0·92 (0·84–1·02)	0·11	0·97 (0·95–0·99)	0·0090
Interleukin-6 (IL-6), per 10^2 x μg/mL	0·17 (0·11–0·27)	<0·0001	1·00 (0·92–1·09)	0·97
Ferritin, per 10^3 x ng/mL	0·19 (0·11–0·31)	<0·0001	1·30 (0·89–1·89)	0·17
CARDIOVASCULAR				
Heart rate per minute, per unit	1·00 (0·99–1·01)	0·69	1·01 (1·00–1·02)	0·15
Systolic blood pressure, per 1 x mmHg	1·00 (0·99–1·00)	0·56	1·00 (0·99–1·00)	0·62
Diastolic blood pressure, per 1 x mmHg	1·02 (1·01–1·04)	<0·0001	1·02 (1·01–1·03)	<0·0001
RESPIRATORY TRACT				
Chest pain	1·45 (0·86–2·38)	0·16	0·98 (0·61–1·59)	0·94
Dyspnoea	0·19 (0·13–0·27)	<0·0001	0·65 (0·48–0·88)	0·0061
Cough	1·22 (0·87–1·72)	0·25	1·61 (1·19–2·22)	0·0021
Expectoration	0·46 (0·32–0·68)	<0·0001	0·74 (0·53–1·01)	0·055
Haemoptysis	0·51 (0·20–1·30)	0·16	0·48 (0·22–1·04)	0·062
Respiratory rate per minute, per unit	0·80 (0·77–0·83)	<0·001	0·94 (0·92–0·97)	<0·0001

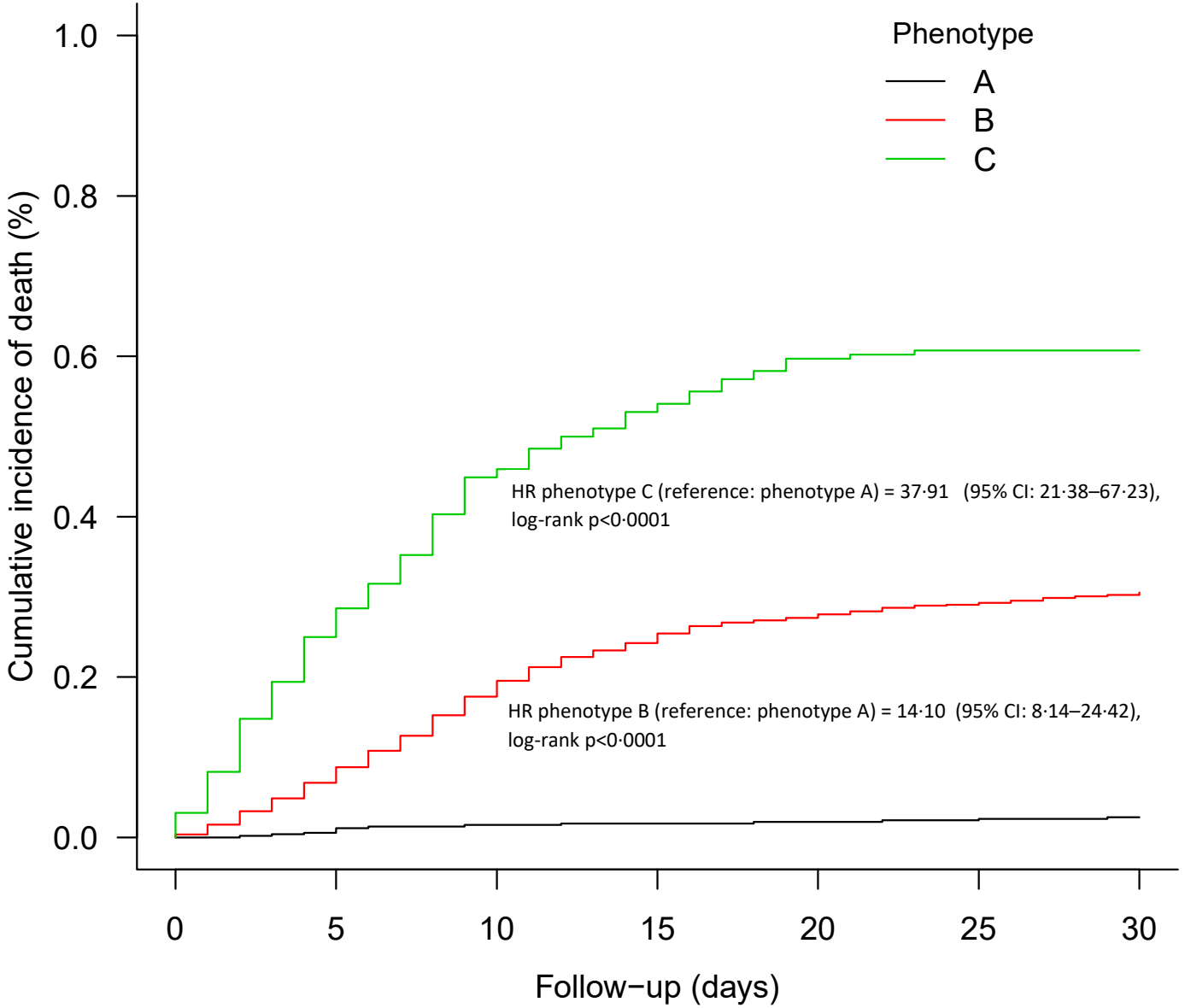
Oxygen saturation (room air, pulse oximetry), per 1 %	1·62 (1·55–1·70)	<0·0001	1·09 (1·07–1·11)	<0·0001
Oxygen saturation after oxygen supplementation, per 1%	1·35 (1·26–1·45)	<0·0001	1·07 (1·03–1·11)	<0·0001
Oxygen saturation (room air, venous blood), per 1%	1·07 (1·05–1·09)	<0·0001	1·03 (1·02–1·03)	<0·0001
PCO_2, venous blood, per 1 x mmHg	1·01 (0·99–1·02)	0·61	0·98 (0·96–0·99)	0·022
Lung infiltrates on chest radiography				
No infiltrate	3·43 (2·32–5·08)	<0·0001	0·77 (0·54–1·10)	0·15
Unilateral	2·25 (1·44–3·51)	<0·0001	1·16 (0·78–1·72)	0·45
Bilateral	Reference		Reference	
Interstitial lung infiltrate	0·48 (0·34–0·68)	<0·0001	1·18 (0·88–1·59)	0·27
Ground–glass opacity infiltrate	0·74 (0·43–1·25)	0·26	1·19 (0·75–1·85)	0·46
LIVER				
Albumin, mean (SD), per 1 x g/dL	9·81 (6·46–14·87)	<0·0001	3·37 (2·37–4·79)	<0·0001
Lactic acid dehydrogenase, per 10^2 x U/L	0·61 (0·55–0·68)	<0·0001	1·00 (0·96–1·04)	1·00
Bilirubin, per 1 x mg/dL	0·93 (0·77–1·13)	0·49	1·00 (0·96–1·04)	0·87
RENAL				
Creatinine, per 1 x mg/dL	0·10 (0·07–0·15)	<0·0001	0·13 (0·10–0·17)	<0·0001
Sodium, per 1 x mEq/L	1·07 (1·03–1·11)	0·0011	1·00 (0·97–1·04)	0·78
Potassium, per 1 x mEq/L	0·25 (0·18–0·34)	<0·0001	0·24 (0·18–0·31)	<0·0001
HEMATOLOGICAL				
Haemoglobin, per 1 x g/dL	1·66 (1·53–1·81)	<0·0001	1·60 (1·48–1·72)	<0·0001
Haematocrit, per 1 %	1·19 (1·15–1·23)	<0·0001	1·16 (1·13–1·20)	<0·0001
Platelets, per 10^5/µL	0·86 (0·76–0·99)	0·031	0·80 (0·71–0·90)	<0·0001
Activated partial thromboplastin time, per 1 x sec	0·99 (0·98–1·00)	0·038	0·99 (0·99–1·00)	0·075
International normalised ratio, per unit·	0·18 (0·12–0·28)	<0·0001	0·32 (0·26–0·40)	<0·0001
OTHER				
Creatine phosphokinase, per 10^2 x U/L	1·01 (0·95–1·08)	0·71	1·02 (0·96–1·08)	0·50
Blood glucose, per 1 x mg/dL	0·98 (0·98–0·98)	<0·0001	0·99 (0·99–0·99)	<0·0001

Table 2. Multinomial logistic regression model for the prediction of phenotypes in the derivation cohort. The reference category is phenotype C. The variance inflation factor value was <2 in all cases.

	Phenotype A vs phenotype C		**Phenotype B vs phenotype C**	
	OR (95% CI)[2]	**P value**	**OR (95% CI)[2]**	**P value**
Age, per year	0·93 (0·90–0·96)	<0·0001	0·96 (0·93–0·99)	0·0051
Female gender	0·68 (0·33–1·41)	0·30	0·44 (0·22–0·89)	0·021
Chronic lung disease	0·55 (0·26–1·16)	0·10	0·79 (0·42–1·54)	0·48
Obesity (BMI>30)	0·49 (0·20–1·23)	0·12	0·71 (0·31–1·64)	0·42
White blood cells, per 10^3 cells/µL	0·80 (0·73–0·87)	<0·0001	0·73 (0·68–0·79)	<0·0011
Neutrophils, per 10^3 cells/µL	0·89 (0·80–0·99)	0·032	0·99 (0·90–1·08)	0·86
C reactive protein, per 10^2 mg/L	0·95 (0·91–1·00)	0·055	0·94 (0·90–0·99)	0·011
Diastolic blood pressure, per 1 mmHg	1·03 (1·01 –1·05)	0·011	1·02 (1·01–1·04)	0·013
Oxygen saturation (room air, pulse oximetry), per 1 %	1·56 (1·46–1·66)	<0·0001	1·11 (1·07–1·16)	<0·0001
Lung infiltrate on chest radiography				
No infiltrate	4·07 (1·83–9·02)	0·00055	1·17 (0·55–2·49)	0·69
Unilateral	3·50 (1·51–8·06)	0·0032	2·05 (0·93–4·51)	0·071
Bilateral	Reference		Reference	
Creatinine, per 1 mg/dL	0·09 (0·05–0·15)	<0·0001	0·06 (0·04–0·10)	<0·0001
Sodium, per 1 mEq/L	1·09 (1·02–1·17)	0·010	1·04 (0·98–1·11)	0·14
Potassium, per 1 mEq/L	0·37 (0·21–0·67)	0·00093	0·26 (0·15–0·45)	<0·0001
Haematocrit, per 1 %	1·29 (1·21–1·38)	<0·0001	1·27 (1·19–1·35)	<0·0001
International normalised ratio, per unit	0·12 (0·07–0·22)	<0·0001	0·12 (0·08–0·18)	<0·0001
Blood glucose, per 1 mg/dL	0·99 (0·98–0·99)	<0·0001	0·99 (0·98-0·99)	<0·0001

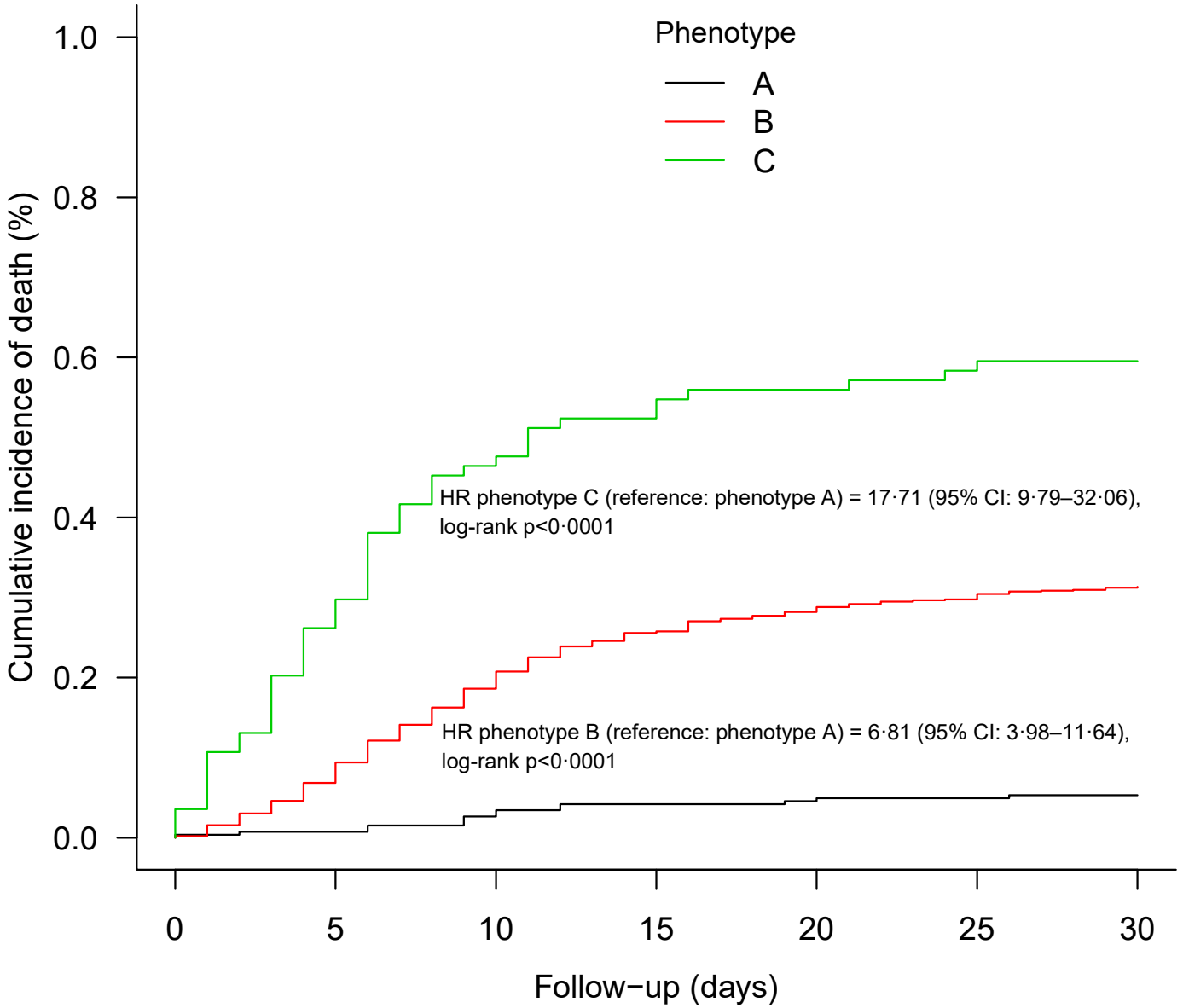

Demographics
Comorbidities
Non−focal
Inflammation
Cardiovascular
Respiratory
Liver
Renal
Hematological
Others
Phenotype A
Phenotype B
Phenotype C


Demographics and Non-focal symptoms
Age
Temperature
Inflammation
White blood cells
Lymphocytes
Neutrophils
D-dimer
Procalcitonin
C reactive protein
Interleukin-6
Ferritin
Cardio-vascular
Heart rate
Systolic blood pressure
Diastolic blood pressure
Respiratory tract
Respiratory rate
Oxygen saturation/room air pulse oximetry
Oxygen saturation/after oxygen supplementation
PCO2
Oxygen saturation/room air, venous blood
Liver
Albumin
LDH
Bilirubin
Renal
Creatinine
Sodium
Potassium
Hematological
Hemoglobin
Hematocrit
Platelets
APTT
INR
Others
CPK
Blood glucose
A
B
C
Phenotype
-1
-0·8
-0·6
-0·4
-0·2
Mean
0·4
0·8
1·2
1·6
2



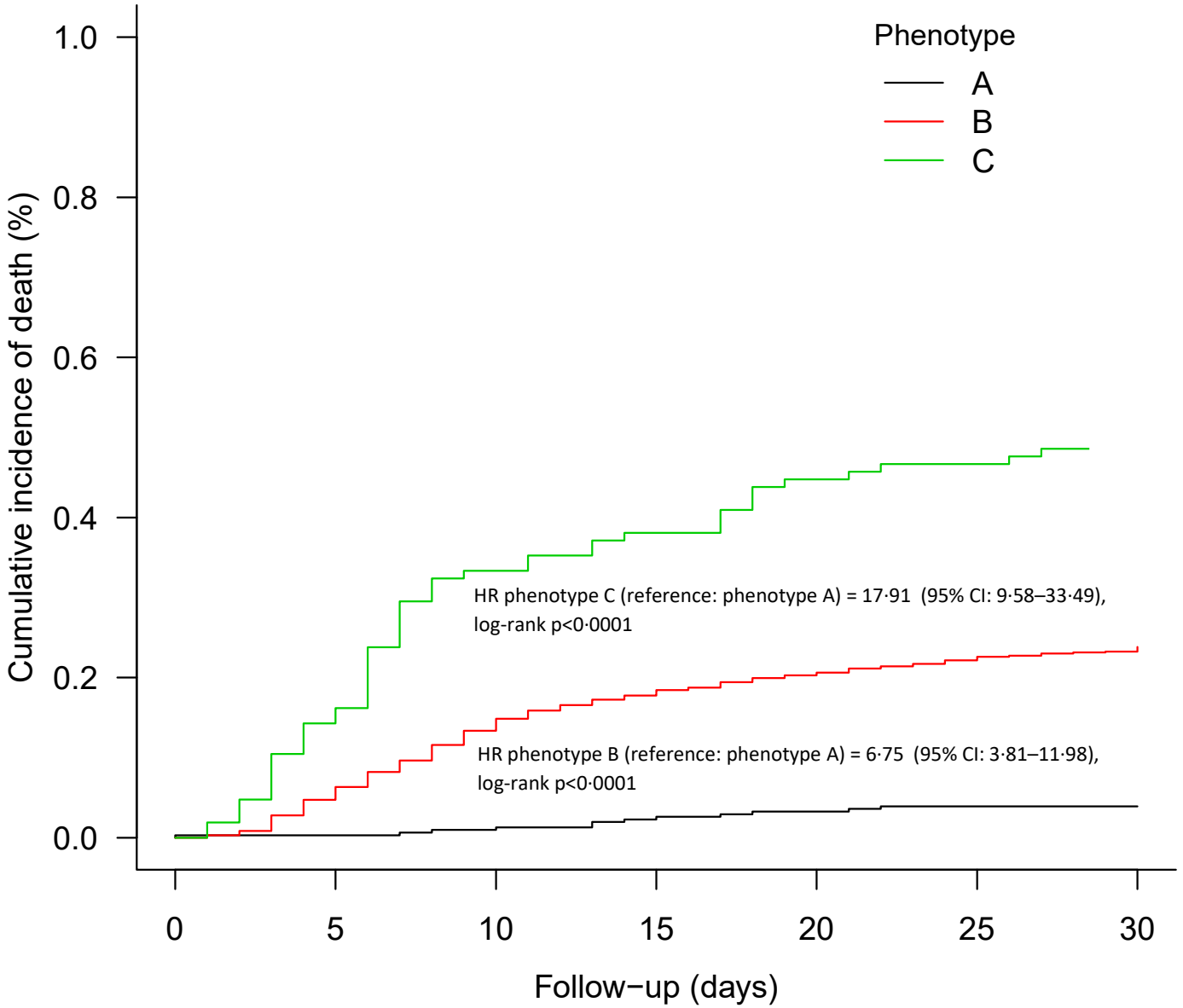
Number at risk

A	516	513	508	507	506	505	503
B	1955	1822	1612	1481	1420	1388	1364
C	196	147	108	92	79	77	77



Number at risk

A	263	261	256	252	251	250	249
B	1021	951	831	760	733	717	702
C	84	62	45	40	37	35	34



Number at risk

A	323	303	301	297	294	292	292
B	1757	1668	1517	1440	1396	1363	1344
C	105	90	70	65	58	56	52

SUPPLEMENTARY APPENDIX

Identification and Validation of Clinical Phenotypes with Outcome Implications in Hospitalized COVID-19 Patients.

Table of contents

1. STROBE Statement—Checklist

	Item No	Recommendation	Section or page in manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	Introduction, last paragraph
Methods			
Study design	4	Present key elements of study design early in the paper	Methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods
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	Methods
Bias	9	Describe any efforts to address potential sources of bias	Discussion (paragraph discussing limitations)
Study size	10	Explain how the study size was arrived at	No sample size calculation
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Methods
		(*b*) Describe any methods used to examine subgroups and interactions	Methods
		(*c*) Explain how missing data were addressed	Methods
		(*d*) If applicable, explain how loss to follow-up was addressed	Not applicable
		(*e*) Describe any sensitivity analyses	Methods
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	This information is included in the referenced publications for the cohorts used
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Figure S1 (appendix)

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Tables 1, S2, S3 and references from cohorts publications
		(b) Indicate number of participants with missing data for each variable of interest	Supplementary Table S1
		(c) Summarise follow-up time (eg, average and total amount)	Methods
Outcome data	15*	Report numbers of outcome events or summary measures over time	Included in the referenced publications for the cohort used
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	Methods and Results, Table 1
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion
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	Discussion
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion
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	Discussion

2. SUPPLEMENTARY METHODS

Chord plots

The patterns of variables distribution are shown as a chord plot; for this plot, the variables were grouped in the following categories (as shown in Table 1): demographics, comorbidities, non-focal symptoms, inflammation, cardiovascular, respiratory tract, liver, renal/ hydroelectrolitic, haematological and others. The phenotypes are depicted in different colours. For each phenotype, if the variable mean (for continuous variables) or proportion (for categorical variables) is significantly higher or lower than the mean or proportion in the full derivation cohort, a ribbon connects the phenotype and the variable group. The width of the ribbons correlates with the number of variables that are significantly higher or lower than the mean or proportion in the full derivation cohort for that phenotype. The Circlize package in R was used to develop the chord plot.

Reference: Gu L, Eils R, Schlesner M, Brors B. Circlize implements and enhances circular visualization in R. Bioinformatics 2014; 30: 2811–2812. https://doi.org/10.1093/bioinformatics/btu393

Heatmaps

In this figures, a colour gradient is used to show the significant difference in mean (continuous variables) in relation to the derivation cohort. The colour gradient indicates the number of standard deviations that the average value in the subcohort of interest is below or above the average value in the full cohort, towards red for higher values and blue for lower values.

Formula applied to calculate the probability of phenotype belonging, based on the multinomial logistic regression probabilistic model

For phenotype A:

$$P_{A=} \frac{\exp(LP_{A)}}{1+\exp(LP_{A)}+\exp(LP_{B)}}$$

Where LP_A (lineal predictor of phenotype A) = $\beta_{0A} + \beta_{1A} * X_1 + \cdots + \beta_{iA} * X_i$

Where $\beta_{0A}\ is\ a\ constant;\ \beta_{1A}, \dots,\ \beta_{iA}$ are the β coefficients obtained in the multinomial model; $X_1,\ldots, X_i$ are the values of the variables included in the model for the specific patient.

For phenotype B:

$$P_{B=} \frac{\exp(LP_{B)}}{1+\exp(LP_{A)}+\exp(LP_{B)}}$$

Where LP_B (lineal predictor of phenotype B) = $\beta_{0B} + \beta_{1B} * X_1 + \cdots + \beta_{iB} * X_i$

Where $\beta_{0B}\ is\ a\ constant;\ \beta_{1B}, \dots,\ \beta_{iB}$ are the β coefficients obtained in the multinomial model; $X_1,\ldots, X_i$ are the values of the variables included in the model for the specific patient.

For phenotype C:

$$P_C = 1 - P_A - P_B$$

3. SUPPLEMENTARY TABLES

Supplementary Table S1. Missing data for the variables collected in the derivation cohort.

Variables	% Missing data
DEMOGRAPHICS	
Age	0·10
Gender	1·19
Race	2·97
COMORBILITIES	
Chronic heart disease	1·02
Hypertension	0·62
Chronic lung disease	0·99
Asthma	0·87
Chronic kidney disease	0·87
Liver cirrhosis	0·92
Chronic neurological Disease	0·82
Active solid malignancy	0·92
Active haematological malignancy	0·74
HIV/AIDS	1·81
Obesity	10·63
Diabetes mellitus	0·82
Chronic inflammatory disease	0·94
Dementia	1·39
Malnutrition	0·72
Smoking status	27·70
TREATMENTS FOR UNDERLYING CONDITIONS	
Angiotensin converting enzyme inhibitors	1·29
Angiotensin receptor blockers	1·19
Inhaled corticosteroids	1·24
Systemic corticosteroids	1·31
Cancer chemotherapy	1·24
"Biological" drugs	1·44
INFECTION DATA AT ADMISSION	
NON-FOCAL SYMPTOMS	
Reported fever	0·87
Temperature	3·82
Myalgia / arthralgia	5·60
Headache	6·07
Skin rash	0·64
Anosmia	21·36
Altered mental status	2·58
INFLAMMATION	
White blood cells	1·59
Neutrophils	1·83
Lymphocytes	1·78
D-dimer	61·3
Procalcitonin	61·00
C reactive protein	8·87
Interleukin-6	93·58
Ferritin, mean	85·48
CARDIOVASCULAR	
Heart rate	4·63
Systolic blood pressure	5·11
Diastolic blood pressure	5·18
RESPIRATORY TRACT	
Chest pain	3·10
Dyspnoea	1·36
Cough	1·26
Expectoration	1·78
Haemoptysis	2·26
Respiratory rate	48·92
Oxygen saturation (room air, pulse oximetry)	12·07
Oxygen saturation after oxygen supplementation	67·56
Oxygen saturation (room air, venous blood)	47·31
PCO_2, venous blood	46·27
Type of lung infiltrate on radiography	7·93
Interstitial lung infiltrate/s	0·30
Ground-glass opacity infiltrate/s	0·30
LIVER	
Albumin	65·03
Lactic acid dehydrogenase	36·11

Bilirubin	34·32
RENAL/ HYDROELECTROLITIC	
Creatinine	2·28
Sodium	2·50
Potassium	4·83
HEMATOLOGICAL	
Haemoglobin	1·36
Haematocrit	2·43
Platelets	1·86
Activated partial thromboplastin time	22·87
International normalised ratio	18·19
OTHERS	
Creatine phosphokinase	69·81
Blood glucose	4·58
COMPLICATIONS DURING HOSPITALIZATION AND PROGNOSIS	
Transfusion-requiring anaemia	0·99
Pleural effusion	0·97
Acute kidney failure	0·87
Heart failure	1·26
Stroke	0·95
Liver failure	1·36
Bacterial pneumonia	2·01
Arrhythmia	1·04
Ischemic coronary even	1·04
Disseminated intravascular coagulation	1·29
Acute respiratory distress syndrome	1·39
Admission to ICU	1·16
Cardiorespiratory arrest	1·12
30-day mortality	0

Table S2. Features and prognosis of patients in the derivation cohort and in the phenotypes obtained.

	All cohort (n=2667)	Phenotype A (n=516)	Phenotype B (n=1955)	Phenotype C (n=196)	P value
DEMOGRAPHICS					
Age, mean (SD), years	66·7 (17·2)	55·2 (18·4)	68·7 (15·9)	77·2 (10·9)	<0·0001
Male gender, no. (%)	1643 (61·6)	285 (55·2)	1223 (62·6)	135 (68·9)	0.00091
Race, no. (%)					0·00080
Caucasian	2434 (91·3)	449 (87·0)	1798 (92·0)	187 (95·4)	
African	6 (0·2)	4 (0·8)	2 (0·1)	0 (0·0)	
Hispanic	165 (6·2)	52 (10·1)	108 (5·5)	5 (2·6)	
Asian	13 (0·5)	1 (0·2)	11 (0·6)	1 (0·5)	
Arab	23 (0·9)	5 (1·0)	16 (0·8)	2 (1·0)	
Other	26 (1·0)	5 (1·0)	20 (1·0)	1 (0·5)	
COMORBIDITIES					
Chronic heart disease, no. (%)	626 (23·5)	68 (13·2)	448 (22·9)	110 (56·1)	<0·0001
Hypertension, no. (%)	1360 (51·0)	161 (31·2)	1031 (52·7)	168 (85·7)	<0·0001
Chronic lung disease, no. (%)	482 (18·1)	40 (7·8)	381 (19·5)	61 (31·1)	<0·0001
Asthma, no. (%)	199 (7·5)	40 (7·8)	150 (7·7)	9 (4·6)	0·28
Chronic kidney disease (stage 4, eGFR <30), no. (%)	136 (5·1)	14 (2·7)	56 (2·9)	66 (33·7)	<0·0001
Liver cirrhosis, no. (%)	42 (1·6)	8 (1·6)	30 (1·5)	4 (2·0)	0·86
Chronic neurological disease, no. (%)	256 (9·6)	36 (7·0)	192 (9·8)	28 (14·3)	0·010
Active solid malignancy, no. (%)	173 (6·5)	29 (5·6)	127 (6·5)	17 (8·7)	0·34
Active haematological malignancy, no (%)	61 (2·3)	11 (2·1)	45 (2·3)	5 (2·6)	0·94
HIV/AIDS, no. (%)	17 (0·6)	2 (0·4)	15 (0·8)	0 (0·0)	0·32
Obesity (BMI>30), no. (%)	357 (13·4)	41 (7·9)	270 (13·8)	46 (3·5)	<0·0001
Diabetes mellitus, no. (%)	587 (22·0)	53 (10·3)	439 (22·5)	95 (48·5)	<0·0001
Chronic inflammatory disease, no. (%)	147 (5·5)	31 (6·0)	107 (5·5)	9 (4·6)	0·75
Dementia, no. (%)	230 (8·6)	17 (3·3)	183 (9·4)	30 (15·3)	<0·0001
Malnutrition, no. (%)	46 (1·7)	4 (0·8)	35 (1·8)	7 (3·6)	0·034
Smoking status					<0·0001
Never, no. (%)	1347 (50·5)	322 (62·4)	941 (48·1)	84 (42·9)	
Present, no. (%)	219 (8·2)	55 (10·7)	149 (7·6)	15 (7·7)	
Former, no. (%)	1101 (41·3)	139 (26·9)	865 (44·2)	97 (49·5)	
TREATMENTS FOR UNDERLYING CONDITIONS					
Angiotensin converting enzyme inhibitors, no. (%)	505 (18·9)	59 (11·4)	397 (20·3)	49 (25·0)	<0·0001
Angiotensin receptor blockers, no. (%)	452 (16·9)	67 (13·0)	333 (17·0)	52 (26·5)	<0·0001
Inhaled corticosteroids, no. (%)	320 (12·0)	36 (7·0)	253 (12·9)	31 (15·8)	0·00024

Systemic corticosteroids, no. (%)	136 (5·1)	23 (4·5)	99 (5·1)	14 (7·1)	0·34
Cancer chemotherapy, no. (%)	76 (2·8)	15 (2·9)	56 (2·9)	5 (2·6)	0·96
"Biological" drugs, no. (%)	62 (2·3)	17 (3·3)	39 (2·0)	6 (3·1)	0·17
INFECTION DATA AT ADMISSION					
NON-FOCAL SYMPTOMS					
Reported fever, no. (%)	2169 (81·3)	414 (80·2)	1620 (82·9)	135 (68·9)	<0·0001
Temperature, mean (SD), ºC	37.21 (0·95)	37·02 (0·89)	37·28 (0·95)	37·08 (0·94)	<0·0001
Myalgia/arthralgia, no. (%)	681 (25·5)	150 (29·1)	505 (25·8)	26 (13·3)	<0·0001
Headache, no. (%)	294 11·0)	98 (19·0)	182 (9·3)	14 (7·1)	<0·0001
Skin rash, no. (%)	29 (1·1)	5 (1·0)	22 (1·1)	2 (1·0)	0·96
Anosmia, no. (%)	40 (1·5)	14 (2·7)	25 (1·3)	1 (0·5)	0·029
Altered mental status, no. (%)	303 (11·4)	27 (5·2)	241 (12·3)	35 (17·9)	<0·0001
INFLAMMATION					
White blood cells, mean (SD), cells/µL	6844 (3982)	6149 (2837)	6575 (3128)	11355 (8659)	<0·0001
Lymphocytes, mean (SD), cells/µL	1161 (1485)	1439 (1761)	1094 (1424)	1096 (1170)	<0·0001
Neutrophils, mean (SD), cells/µL	5009 (3387)	4112 (2511)	4892 (2844)	8539 (6656)	<0·0001
D-dimer, mean (SD),µg/L	960·2 (2928·3)	715·8 (986·5)	986·3 (3290·5)	1343·1 (2419·7)	<0·0001
Procalcitonin, mean (SD), ng/mL	0·28 (0·54)	0·17 (0·26)	0·27 (0·51)	0·70 (0·96)	<0·0001
C reactive protein, mean (SD), mg/L	83·6 (86·9)	47·44 (68·3)	88·8 (84·2)	127·1 (119·8)	<0·0001
Interleukin-6, mean (SD), µg/mL	73·1 (153·7)	50·9 (30·4)	78·3 (177·4)	78·8 (59·0)	<0·0001
Ferritin, mean (SD), ng/mL	768·01 (525·7)	616·39 (219·7)	809·5 (588·4)	752·8 (320·4)	<0·0001
CARDIOVASCULAR					
Heart rate per minute, mean (SD)	87·6 (16·6)	86·8 (16·2)	88·0 (16·6)	86·2 (17·9)	0·051
Systolic blood pressure, mean (SD), mmHg	126·6 (23·5)	125·1 (21·9)	127·1 (23·5)	126·2 (27·9)	0·13
Diastolic blood pressure, mean (SD), mmHg	73·5 (24·7)	74·4 (14·0)	73·7 (27·3)	69·1 (17·9)	0·034
RESPIRATORY TRACT					
Chest pain, no. (%)	303 (11·4)	76 (14·7)	206 (10·5)	21 (10·7)	0·027
Dyspnoea, no. (%)	1326 (49·7)	133 (25·8)	1066 (54·5)	127 (64·8)	<0·0001
Cough, no. (%)	1913 (71·7)	350 (67·8)	1439 (73·6)	124 (63·3)	0·00083
Expectoration, no. (%)	648 (24·3)	91 (17·6)	495 (25·3)	62 (31·6)	<0·001
Haemoptysis, no. (%)	58 (2·2)	11 (2·1)	39 (2·0)	8 (4·1)	0·16
Respiratory rate per minute, mean (SD).	20·4 (5·1)	18·1 (3·3)	20·7 (5·3)	22·9 (5·4)	<0·0001
Oxygen saturation (room air, pulse oximetry), mean (SD), %	92·5 (5·9)	96·54 (2·4)	92·0 (5·2)	86·9 (10·7)	<0·0001
Oxygen saturation after oxygen supplementation, mean (SD), %	95·1 (2·8)	95·8 (1·2)	95·0 (2·9)	94·0 (3·8)	<0·0001
Oxygen saturation (room air, blood), mean (SD), %	90·7 (12·2)	93·5 (9·2)	90·6 (11·4)	83·8 (20·9)	<0·0001
PCO_2, blood, mean (SD), mmHg	39·1 (7·8)	40·3 (5·2)	38·7 (8·2)	39·8 (8·5)	<0·0001

Lung infiltrates on chest radiography <0·0001

Any infiltrate, no (%)	1989 (74·5)	275 (53·2)	1607 (82·1)	147 (75·0)	
Unilateral, no (%)	581 (21·8)	116 (22·5)	429 (21·9)	36 (18·4)	
Bilateral, no (%)	1408 (52·8)	159 (30·8)	1138 (58·2)	111 (56·6)	
Interstitial infiltrate, no· (%)	1087 (40·8)	129 (25·0)	878 (44·9)	80 (40·8)	<0·0001
Ground-glass opacity infiltrate, no (%)	335 (12·6)	46 (8·9)	266 (13·6)	23 (11·7)	0·016
LIVER					
Albumin, mean (SD), g/dL	3·49 (0·41)	3·64 (0·40)	3·47 (0·40)	3·27 (0·40)	<0·0001
Lactic acid dehydrogenase, mean (SD), U/L	336·1 (328·9)	277·7 (117·5)	350·1 (375·1)	350·0 (147·7)	<0·001
Bilirubin, mean (SD), mg/dL	0·68 (2·65)	0·62 (0·63)	0·69 (3·06)	0·73 (0·93)	0·057
RENAL/HYDROELECTROLITIC					
Creatinine, mean (SD), mg/dL	1·11 (0·83)	0·96 (0·56)	0·99 (0·36)	2·76 (2·11)	<0·0001
Sodium, mean (SD), mEq/L	137·5 (4·1)	138·3 (3·5)	137·3 (4·1)	137·2 (5·3)	<0·0001
Potassium, mean (SD), mEq/L	4·1 (0·5)	4·0 (0·5)	4·0 (0·5)	4·5 (0·7)	<0·0001
HEMATOLOGICAL					
Haemoglobin, mean (SD), g/dL	13·4 (1·9)	13·7 (1·7)	13·5 (1·8)	11·5 (2·4)	<0·0001
Haematocrit, mean (SD), %	40·3 (5·4)	41·1 (4·8)	40·5 (5·2)	35·8 (6·5)	<0·0001
Platelets, mean (SD), $x10^3/\mu L$	195·67 (98·90)	203·30 (88·62)	191·12 (97·58)	219·40 (128·89)	0·0001
Activated partial thromboplastin time), mean (SD), sec	28·10 (17·25)	27·23 (10·57)	28·04 (18·58)	30·94 (17·39)	0·037
International normalised ratio, mean (SD)	1·23 (0·56)	1·14 (0·28)	1·19 (0·34)	1·92 (1·57)	<0·0001
OTHERS					
Creatine phosphokinase (CPK), mean (SD), U/L	160·0 (432·4)	150·8 (368·2)	164·3 (464·0)	141·4 (199·0)	0·062
Blood glucose, mean (SD), mg/dL	127·5 (61·5)	109·8 (38·8)	126·6 (49·3)	182·3 (139·7)	<0·0001
COMPLICATIONS DURING HOSPITALISATION AND PROGNOSIS					
Transfusion-requiring anaemia, no. (%)	101 (3·8)	3 (0·6)	75 (3·9)	23 (11·9)	<0·0001
Pleural effusion, no. (%)	92 (3·5)	6 (1·2)	64 (3·3)	22 (11·4)	<0·0001
Acute kidney failure, no. (%)	399 (15·1)	17 (3·3)	307 (15·9)	75 (38·5)	<0·0001
Heart failure, no. (%)	153 (5·8)	3 (0·6)	113 (5·9)	37 (19·2)	<0·0001
Stroke, no (%)	18 (0·7)	4 (0·8)	12 (0·6)	2 (1·0)	0·76
Liver failure, no (%)	76 (2·9)	8 (1·6)	61 (3·2)	7 (3·6)	0·13
Bacterial pneumonia, no (%)	271 (10·2)	10 (1·9)	228 (11·7)	33 (16·8)	<0·0001
Ischemic coronary event, no (%)	21 (0·8)	2 (0·4)	16 (0·8)	3 (1·5)	0·29
Disseminated intravascular coagulation, no (%)	27 (1·0)	2 (0·4)	21 (1·1)	4 (2·0)	0·12

Acute respiratory distress syndrome, no (%)	831 (31·2)	7 (1·4)	735 (37·6)	89 (45·4)	<0·0001
Admission to ICU, no (%)	474 (17·8)	9 (1·7)	433 (22·1)	32 (16·3)	<0·0001
Cardiorespiratory arrest, no (%)	242 (9·2)	5 (1·0)	192 (9·9)	45 (23·2)	<0·0001
30-day mortality, no (%)	729 (27·3)	13 (2·5)	597 (30·5)	119 (60·7)	<0·0001

Supplementary Table S3. Features of patients in phenotypes in the internal validation cohort. The phenotypes were directly derived from this cohort with the same methodology used to derive the phenotypes from the derivation cohort.

	All cohort (n=1368)	Phenotype A (n=233)	Phenotype B (n=1019)	Phenotype C (n=116)	P value
DEMOGRAPHICS					
Age, mean (SD), years	66·84 (16·90)	53·94 (17·78)	68·94 (15·37)	74·34 (15·32)	<0·0001
Male gender, no. (%)	819 (59·9)	117 (50·2)	639 (62·7)	63 (54·3)	0·00093
Race, no. (%)					0·030
Caucasian	1249 (91·3)	201 (86·3)	938 (92·1)	110 (94·8)	
African	6 (0·4)	1 (0·4)	5 (0·5)	0 (0·0)	
Hispanic	88 (6·4)	23 (9·9)	59 (5·8)	6 (5·2)	
Asian	7 (0·5)	0 (0·0)	7 (0·7)	0 (0·0)	
Arab	10 (0·7)	5 (2·1)	5 (0·5)	0 (0·0)	
Other	8 (0·6)	3 (1·3)	5 (0·5)	0 (0·0)	
COMORBIDITIES					
Chronic heart disease, no. (%)	316 (23·1)	18 (7·7)	252 (24·7)	46 (39·7)	<0·0001
Hypertension, no. (%)	703 (51·4)	66 (28·3)	552 (54·2)	85 (73·3)	<0·0001
Chronic lung disease, no. (%)	239 (17·5)	14 (6·0)	193 (18·9)	32 (27·6)	<0·0001
Asthma, no. (%)	101 (7·4)	16 (6·9)	78 (7·7)	7 (6·0)	0·77
Chronic kidney disease (stage 4, eGFR <30), no. (%)	66 (4·8)	1 (0·4)	29 (2·8)	36 (31·0)	<0·0001
Liver cirrhosis, no. (%)	14 (1·0)	3 (1·3)	7 (0·7)	4 (3·4)	0·022
Chronic neurological disease, no. (%)	124 (9·1)	11 (4·7)	99 (9·7)	14 (12·1)	0·028
Active solid malignancy, no. (%)	95 (6·9)	12 (5·2)	68 (6·7)	15 (12·9)	0·020
Active haematological malignancy, no (%)	34 (2·5)	1 (0·4)	30 (2·9)	3 (2·6)	0·081
HIV/AIDS, no (%)	9 (0·7)	4 (1·7)	5 (0·5)	0 (0·0)	0·070
Obesity (BMI>30), no. (%)	202 (14·8)	22 (9·4)	159 (15·6)	21 (18·1)	0·031
Diabetes mellitus, no. (%)	287 (21·0)	22 (9·4)	218 (21·4)	47 (40·5)	<0·0001
Chronic inflammatory disease, no· (%)	84 (6·1)	11 (4·7)	66 (6·5)	7 (6·0)	0·60
Dementia, no. (%)	100 (7·3)	9 (3·9)	71 (7·0)	20 (17·2)	<0·0001
Malnutrition, no. (%)	19 (1·4)	0 (0·0)	13 (1·3)	6 (5·2)	0·002
Smoking status					0·0001
Never, no. (%)	722 (52·8)	155 (66·5)	509 (50·0)	58 (50·0)	
Present, no. (%)	103 (7·5)	17 (7·3)	76 (7·5)	10 (8·6)	
Former, no. (%)	543 (39·7)	61 (26·2)	434 (42·6)	48 (41·4)	
TREATMENTS FOR UNDERLYING CONDITIONS					
Angiotensin converting enzyme inhibitors, no. (%)	272 (19·9)	27 (11·6)	220 (21·6)	25 (21·6)	0·0023

Angiotensin receptor blockers, no. (%)	250 (18·3)	20 (8·6)	196 (19·2)	34 (29·3)	<0·0001
Inhaled corticosteroids, no. (%)	171 (12·5)	15 (6·4)	135 (13·2)	21 (18·1)	0·0029
Systemic corticosteroids, no. (%)	72 (5·3)	9 (3·9)	50 (4·1)	13 (11·2)	0·0091
Cancer chemotherapy, no. (%)	32 (2·3)	1 (0·4)	27 (2·6)	4 (3·4)	0·10
"Biological" drugs, no. (%)	34 (2·5)	5 (2·1)	23 (2·3)	6 (5·2)	0·15
INFECTION DATA AT ADMISSION					
NON-FOCAL SYMPTOMS					
Reported fever, no. (%)	1105 (80·8)	176 (75·5)	850 (83·4)	79 (68·1)	<0·0001
Temperature, mean (SD), ºC	37·19 (0·96)	37·04 (0·94)	37·25 (0·96)	36·92 (0·98)	0·0002
Myalgia/arthralgia, no. (%)	356 (26·0)	70 (30·0)	264 (25·9)	22 (19·0)	0·084
Headache, no. (%)	140 (10·2)	31 (13·3)	105 (10·3)	4 (3·4)	0·016
Skin rash, no. (%)	23 (1·7)	4 (1·7)	16 (1·6)	3 (2·6)	0·78
Anosmia, no. (%)	32 (2·3)	12 (5·2)	18 (1·8)	2 (1·7)	0·0078
Altered mental status, no. (%)	159 (11·6)	18 (7·7)	119 (11·7)	22 (19·0)	0·0085
INFLAMMATION					
White blood cells, mean (SD), cells/µL	6824·57 (3823·79)	6034·41 (2511·06)	6580·70 (3313·81)	10553·91 (6932·07)	<0·0001
Lymphocytes, mean (SD), cells/µL	1122·85 (1383·84)	1355·79 (799·10)	1034·44 (778·38)	1431·55 (3979·53)	<0·0001
Neutrophils, mean (SD), cells/µL	5069·68 (3458·08)	4070·83 (2201·27)	4915·53 (2947·96)	8430·19 (6466·81)	<0·0001
D-dimer, mean (SD),µg/L	908·7 (1556·7)	669·4 (498·1)	950·0 (1741·5)	1026·0 (1146·7)	0·032
Procalcitonin, mean (SD), ng/mL	0·31 (0·63)	0·16 (0·18)	0·29 (0·60)	0·75 (1·13)	<0·0001
C reactive protein, mean (SD), mg/L	83·9 (90·6)	43·7 (66·2)	86·1 (83·9)	145·8 (138·7)	<0·0001
Interleukin-6, mean (SD), µg/mL	76·6 (198·4)	50·7 (29·1)	83·1 (228·7)	71·6 (37·8)	0·076
Ferritin, mean (SD), ng/mL	771·7 (565·6)	611·5 (224·3)	798·6 (606·4)	857·1 (617·1)	<0·0001
CARDIOVASCULAR					
Heart rate per minute, mean (SD)	86·8 (16·7)	85·0 (16·1)	86·9 (16·4)	89·3 (20·0)	0·066
Systolic blood pressure, mean (SD), mmHg	126·4 (24·1)	120·3 (21·7)	127·1 (23·8)	132·0 (28·9)	<0·0001
Diastolic blood pressure, mean (SD), mmHg	73·1 (15·7)	74·8 (13·9)	73·3 (16·0)	67·6 (15·7)	<0·0001
RESPIRATORY TRACT					
Chest pain, no. (%)	136 (9·9)	29 (12·4)	97 (9·5)	10 (8·6)	0·36
Dyspnoea, no. (%)	660 (48·2)	57 (24·5)	532 (52·2)	71 (61·2)	<0·0001
Cough, no. (%)	999 (73·0)	165 (70·8)	756 (74·2)	78 (67·2)	0·20
Expectoration, no. (%)	330 (24·1)	42 (18·0)	260 (25·5)	28 (24·1)	0·055
Haemoptysis, no. (%)	41 (3·0)	6 (2·6)	33 (3·2)	2 (1·7)	0·61
Respiratory rate per minute, mean (SD).	20·4 (4·9)	18·1 (3·0)	20·6 (4·9)	22·7 (6·5)	<0·0001
Oxygen saturation (room air, pulse oximetry), mean (SD), %	92·6 (5·6)	96·6 (2·1)	92·0 (5·3)	89·8 (8·0)	<0·0001
Oxygen saturation after oxygen supplementation, mean (SD), %	95·1 (2·3)	96·0 (0·9)	95·1 (2·2)	94·2 (4·1)	<0·0001

Oxygen saturation (room air, venous blood), mean (SD), %	91·00 (10·95)	94·71 (3·66)	90·80 (10·72)	85·28 (17·88)	<0·0001
PCO_2, venous blood, mean (SD), mmHg	38·77 (6·72)	40·07 (4·60)	38·26 (6·59)	40·65 (9·97)	<0·0001
Lung infiltrates on chest radiography					<0·0001
Any infiltrate, no (%)	1013 (74·0)	117 (50·2)	811 (79·5)	85 (73·2)	
Unilateral, no (%)	280 (20·5)	51 (21·9)	211 (20·7)	18 (15·5)	
Bilateral, no (%)	733 (53·6)	66 (28·3)	600 (58·9)	67 (57·8)	
Interstitial infiltrate, no· (%)	579 (42·3)	65 (27·9)	463 (45·4)	51 (44·0)	<0·0001
Ground-glass opacity infiltrate, no (%)	158 (11·5)	26 (11·2)	124 (12·2)	8 (6·9)	0·24
LIVER					
Albumin, mean (SD), g/dL	3·49 (0·41)	3·67 (0·42)	3·47 (0·40)	3·35 (0·34)	<0·0001
Lactic acid dehydrogenase, mean (SD), U/L	336·7 (177·5)	274·1 (120·9)	347·3 (185·7)	369·2 (172·8)	<0·0001
Bilirubin, mean (SD), mg/dL	0·70 (1·66)	0·61 (0·34)	0·73 (1·91)	0·68 (0·49)	0·60
RENAL/HYDROELECTROLITIC					
Creatinine, mean (SD), mg/dL	1·09 (0·78)	0·87 (0·31)	0·99 (0·37)	2·40 (1·98)	<0·0001
Sodium, mean (SD), mEq/L	137·4 (4·2)	138·4 (3·3)	137·2 (4·2)	137·3 (5·9)	<0·0001
Potassium, mean (SD), mEq/L	4·11 (0·55)	4·05 (0·44)	4·09 (0·53)	4·49 (0·69)	<0·0001
HEMATOLOGICAL					
Haemoglobin, mean (SD), g/dL	13·3 (1·9)	13·6 (1·6)	13·5 (1·9)	11·5 (2·2)	<0·0001
Haematocrit, mean (SD), %	40·2 (5·5)	40·7 (4·8)	40·5 (5·4)	35·8 (6·0)	<0·0001
Platelets, mean (SD), $x10^3/\mu L$	197·00 (99·12)	209·79 (91·17)	192·88 (99·19)	207·50 (111·06)	0·031
Activated partial thromboplastin time), mean (SD), sec	28·07 (11·28)	27·34 (9·62)	27·95 (10·89)	30·59 (16·38)	0·032
International normalised ratio, mean (SD)	1·27 (0·75)	1·13 (0·30)	1·20 (0·38)	2·14 (2·11)	<0·0001
OTHERS					
Creatine phosphokinase (CPK), mean (SD), U/L	145·6 (286·2)	114·8 (60·0)	150·6 (318·1)	163·5 (261·2)	0·18
Blood glucose, mean (SD), mg/dL	125·2 (53·5)	105·4 (28·2)	124·7 (45·2)	169·8 (107·6)	<0·0001
COMPLICATIONS DURING HOSPITALIZATION AND PROGNOSIS					
Transfusion-requiring anaemia, no· (%)	47 (3·5)	1 (0·4)	33 (3·3)	13 (11·5)	<0·0001
Pleural effusion, no· (%)	49 (3·6)	1 (0·4)	39 (3·9)	9 (7·8)	0·0017
Acute kidney failure, no· (%)	219 (16·1)	4 (1·7)	174 (17·2)	41 (36·0)	<0·0001
Heart failure, no· (%)	77 (5·7)	0 (0·0)	55 (5·5)	22 (19·3)	<0·0001
Stroke, no (%)	8 (0·6)	0 (0·0)	7 (0·7)	1 (0·9)	0·42
Liver failure, no (%)	28 (2·1)	0 (0·0)	26 (2·6)	2 (1·8)	0·044
Bacterial pneumonia, no (%)	150 (11·0)	6 (2·6)	122 (12·0)	22 (19·0)	<0·0001
Ischemic coronary event, no (%)	11 (0·8)	1 (0·4)	9 (0·9)	1 (0·9)	0·78

Disseminated intravascular coagulation, no (%)	18 (1·3)	0 (0·0)	16 (1·6)	2 (1·7)	0·15
Acute respiratory distress syndrome, no (%)	443 (32·4)	1 (0·4)	392 (38·5)	50 (43·1)	<0·0001
Admission to ICU, no (%)	263 (19·2)	1 (0·4)	238 (23·4)	24 (20·7)	<0·0001
Cardiorespiratory arrest, no (%)	122 (9·0)	0 (0·0)	98 (9·7)	24 (21·2)	<0·0001
30-day mortality, no (%)	384 (28·1)	6 (2·6)	316 (31·0)	62 (53·4)	<0·0001

Supplementary Table S4. Predictive capacity of the multinomial logistic regression model for observed data in the derivation cohort and in different subcohorts obtained randomly from it.

Cohort/Subcohorts in Derivation Cohort (DC) where the model was validated	Predictive capacity to identify phenotype:	AUROC (CI 95%)
GLOBAL derivation cohort (2,667 cases)	A	0·86 (0·85–0·88)
	B	0·88 (0·86–0·89)
	C	0·99 (0·99–0·99)
20 randomly obtained subcohorts with 80% of the derivation sample size (2,134 cases each)	A	Minimum value: 0·83 Mean value: 0·84 Maximum value: 0·85
	B	Minimum value: 0·87 Mean value: 0·88 Maximum value: 0·89
	C	Minimum value: 0·98 Mean value: 0·99 Maximum value: 0·99
20 randomly obtained subcohorts with 60% of the derivation sample size (1,600 cases each)	A	Minimum value: 0·82 Mean value: 0·84 Maximum value: 0·86
	B	Minimum value: 0·86 Mean value: 0·88 Maximum value: 0·89
	C	Minimum value: 0·98 Mean value: 0·99 Maximum value: 0·99
20 randomly obtained subcohorts with 40% of the derivation sample size (1,067 cases each)	A	Minimum value: 0·82 Mean value: 0·84 Maximum value: 0·86
	B	Minimum value: 0·86 Mean value: 0·88 Maximum value: 0·90
	C	Minimum value: 0·98 Mean value: 0·99 Maximum value: 0·99

Supplementary Table S5. Characteristics and prognosis of patients in the internal validation cohort, according to the phenotypes assigned by the probabilistic model.

	Assigned to phenotype A (n=263)	Assigned to phenotype B (n=1021)	Assigned to phenotype C (n=84)	P value
DEMOGRAPHICS				
Age, mean (SD), y	49·63 (16·51)	70·38 (14·19)	77·75 (12·48)	<0·0001
Male gender, no. (%)	123 (46·8)	647 (63·4)	49 (58·3)	<0·0001
Race, no. (%)				0·0096
Caucasian	222 (84·4)	948 (92·9)	79 (94·0)	
African	3 (1·1)	3 (0·3)	0 (0·0)	
Hispanic	29 (11·0)	54 (5·3)	5 (6·0)	
Asian	2 (0·8)	5 (0·5)	0 (0·0)	
Arab	3 (1·1)	7 (0·7)	0 (0·0)	
Other	4 (1·5)	4 (0·4)	0 (0·0)	
COMORBIDITIES				
Chronic heart disease, no. (%)	21 (8·0)	252 (24·7)	43 (51·2)	<0·0001
Hypertension, no. (%)	68 (25·9)	571 (55·9)	64 (76·2)	<0·0001
Chronic lung disease, no. (%)	7 (2·7)	204 (20·0)	28 (33·3)	<0·0001
Asthma, no. (%)	25 (9·5)	74 (7·2)	2 (2·4)	0·089
Chronic kidney disease (stage 4, eGFR <30), no. (%)	6 (2·3)	30 (2·9)	30 (35·7)	<0·0001
Liver cirrhosis, no. (%)	2 (0·8)	10 (1·0)	2 (2·4)	0·42
Chronic neurological disease, no. (%)	11 (4·2)	101 (9·9)	12 (14·3)	0·0036
Active solid malignancy, no. (%)	13 (4·9)	73 (7·1)	9 (10·7)	0·17
Active haematological malignancy, no (%)	3 (1·1)	27 (2·6)	4 (4·8)	0·14
HIV/AIDS, no (%)	7 (2·7)	2 (0·2)	0 (0·0)	< 0·0001
Obesity (BMI>30), no. (%)	20 (7·6)	165 (16·2)	17 (20·2)	0·00076
Diabetes mellitus, no. (%)	20 (7·6)	229 (22·4)	38 (45·2)	<0·0001
Chronic inflammatory disease, no. (%)	12 (4·6)	64 (6·3)	8 (9·5)	0·24
Dementia, no. (%)	5 (1·9)	76 (7·4)	19 (22·6)	<0·0001
Malnutrition, no. (%)	1 (0·4)	14 (1·4)	4 (4·8)	0·022
Smoking status				<0·0001
Never, no. (%)	170 (64·6)	513 (50·2)	39 (46·4)	
Yes, no. (%)	32 (12·2)	63 (6·2)	8 (9·5)	
Former smoker, no. (%)	61 (23·2)	445 (43·6)	37 (44·0)	
TREATMENTS FOR UNDERLYING CONDITIONS				
Angiotensin converting enzyme inhibitors, no. (%)	31 (11·8)	222 (21·7)	19 (22·6)	0·0012
Angiotensin receptor blockers, no. (%)	23 (8·7)	201 (19·7)	26 (31·0)	<0·0001
Inhaled corticosteroids, no. (%)	17 (6·5)	139 (13·6)	15 (17·9)	0·0023
Systemic corticosteroids, no. (%)	16 (6·1)	45 (4·4)	11 (13·1)	0·0022
Cancer chemotherapy, no. (%)	6 (2·3)	25 (2·4)	1 (1·2)	0·76
"Biological" drugs, no. (%)	11 (4·2)	20 (2·0)	3 (3·6)	0·10
INFECTION DATA AT ADMISSION				
NON-FOCAL SYMPTOMS				
Fever, no. (%)	201 (76·4)	849 (83·2)	55 (65·5)	<0·0001
Temperature, mean (SD), ºC	37·1 (0·9)	37·2 (0·9)	37·0 (0·9)	0·13
Myalgia/arthralgia, no. (%)	69 (26·2)	268 (26·2)	19 (22·6)	0·76
Headache, no. (%)	40 (15·2)	96 (9·4)	4 (4·8)	0·0050
Skin rash, no. (%)	4 (1·5)	18 (1·8)	1 (1·2)	0·13
Anosmia, no. (%)	13 (4·9)	18 (1·8)	1 (1·2)	0·0075
Altered mental status, no. (%)	17 (6·5)	125 (12·2)	17 (20·2)	0·0013
INFLAMMATION				
White blood cells, mean (SD), cells/µL	6235·2 (3497·9)	6670·3 (3439·8)	10544·4 (6432·8)	<0·0001
Lymphocytes, mean (SD), cells/µL	1385·1 (909·4)	1023·0 (752·7)	1514·8 (4633·6)	<0·0001
Neutrophils, mean (SD), cells/µL	4086·2 (2869·6)	5057·7 (3152·9)	8294·0 (5932·9)	<0·0001
D-dimer, mean (SD),µg/L	751·1 (931·4)	934·0 (1708·7)	1093·6 (1082·8)	0·13
Procalcitonin, mean (SD), ng/mL	0·23 (0·55)	0·30 (0·61)	0·70 (0·94)	<0·0001
C reactive protein, mean (SD), mg/L	48·6 (76·)	85·9 (82·1)	171·3 (149·5)	<0·0001
Interleukin-6, mean (SD), µg/mL	55·7 (43·5)	82·6 (228·2)	68·8 (21·7)	0·14
Ferritin, mean (SD), ng/mL	651·1 (456·5)	802·5 (589·6)	774·3 (530·5)	0·0001
CARDIOVASCULAR				
Heart rate per minute, mean (SD)	86·8 (16·6)	86·8 (16·7)	87·69 (17·7)	0·78
Systolic blood pressure, mean (SD), mmHg	120·16 (20·81)	127·73 (24·4)	129·9 (26·7)	<0·0001
Diastolic blood pressure, mean (SD), mmHg	75·4 (13·4)	73·0 (16·2)	66·2 (15·2)	<0·0001
PULMONARY				
Chest pain, no. (%)	35 (13·3)	93 (9·1)	8 (9·5)	0·13

Dyspnoea, no. (%)	84 (31·9)	523 (51·2)	53 63·1)	<0·0001
Cough, no. (%)	192 (73·0)	745 (73·0)	62 (73·8)	0·99
Expectoration, no. (%)	53 (20·2)	255 (25·0)	22 (26·2)	0·24
Haemoptysis, no. (%)	8 (3·0)	33 (3·2)	0 (0·0)	0·25
Respiratory rate per minute, mean (SD).	18·5 (5·5)	20·6 (4·5)	22·96 (6·30)	<0·0001
Oxygen saturation (room air, pulse oximetry), mean (SD), %	97·4 (1·6)	91·8 (5·1)	87·7 (9·0)	<0·0001
Oxygen saturation after oxygen supplementation, mean (SD), %	96·1 (1·0)	95·0 (2·5)	94·3 (2·8)	<0·0001
PCO_2, venous blood, mean (SD), mmHg	39·9 (5·2)	38·3 (6·6)	39·8 (10·1)	0·0010
Oxygen saturation (room air, venous blood), mean (SD), %	93·4 (9·2)	90·6 (10·9)	87·5 (13·9)	<0·0001
Lung infiltrates on chest radiography				<0·0001
No infiltrate	155 (58·9)	181 (17·7)	19 (22·6)	
Unilateral	62 (23·6)	210 (20·6)	8 (9·5)	
Bilateral	46 (17·5)	630 (61·7)	57 (67·9)	
Interstitial lung infiltrate, no. (%)	53 (20·2)	480 (47·0)	46 (54·8)	<0·0001
Ground-glass opacity infiltrate, no. (%)	20 (7·6)	130 (12·7)	8 (9·5)	0·057
LIVER				
Albumin, mean (SD), g/dL	3·68 (0·43)	3·46 (0·39)	3·32 (0·35)	<0·0001
Lactic acid dehydrogenase (LDH), mean (SD), U/L	286·50 (226·70)	345·50 (158·47)	387·75 (191·83)	<0·0001
Bilirubin, mean (SD), mg/dL	0·61 (0·33)	0·73 (1·91)	0·65 (0·53)	0·76
RENAL/HYDROELECTROLITIC				
Creatinine, mean (SD), mg/dL	0·91 (0·43)	1·01 (0·41)	2·64 (2·18)	<0·0001
Sodium, mean (SD), mEq/L	138·42 (3·12)	137·20 (4·28)	136·99 (6·47)	<0·0001
Potassium, mean (SD), mEq/L	4·11 (0·46)	4·08 (0·53)	4·49 (0·74)	<0·0001
HEMATOLOGICAL				
Haemoglobin, mean (SD), g/dL	13·6 (1·7)	3·5 (1·9)	11·2 (2·0)	<0·0001
Haematocrit, mean (SD), %	41·1 (4·9)	40·4 (5·4)	34·3 (5·8)	<0·0001
Platelets, mean (SD), $x10^3/\mu L$	209·1 (89·9)	193·1 (101·2)	205·2 (98·0)	0·052
Activated partial thromboplastin time, mean (SD), sec	27·8 (9·9)	27·8 (10·9)	32·0 (17·3)	0·0043
International normalised ratio, mean (SD)·	1·15 (0·43)	1·20 (0·37)	2·49 (2·34)	<0·0001
OTHER				
Creatine phosphokinase, mean (SD), U/L	144·3 (252·5)	145·4 (298·3)	152·6 (231·7)	0·26
Blood glucose, mean (SD), mg/dL	103·8 (32·9)	126·7 (46·7)	174·6 (114·2)	<0·0001
COMPLICATIONS DURING HOSPITALIZATION AND PROGNOSIS				
Transfusion-requiring anaemia, no. (%)	7 (2·7)	32 (3·2)	8 (9·9)	0·0063
Pleural effusion, no. (%)	5 (1·9)	37 (3·7)	7 (8·4)	0·022
Acute kidney failure, no. (%)	11 (4·2)	174 (17·2)	34 (41·5)	<0·0001
Heart failure, no. (%)	3 (1·1)	58 (5·8)	16 (19·5)	<0·0001
Stroke, no (%)	1 (0·4)	6 (0·6)	1 (1·2)	0·69
Liver failure, no. (%)	1 (0·4)	25 (2·5)	2 (2·4)	0·10
Bacterial pneumonia, no. (%)	12 (4·6)	125 (12·2)	13 (15·5)	0·00071
Arrhythmia, no. (%)	6 (2·3)	39 (3·8)	4 (4·8)	0·41
Ischemic coronary event, no. (%)	2 (0·8)	8 (0·8)	1 (1·2)	0·92
Disseminated intravascular coagulation, no. (%)	0 (0·0)	16 (1·6)	2 (2·4)	0·094
Acute respiratory distress syndrome, no. (%)	24 (9·1)	374 (36·6)	45 (53·6)	<0·0001
Admission to ICU, no. (%)	20 (7·6)	226 (22·1)	17 (20·2)	<0·0001
Cardiorespiratory arrest, no. (%)	6 (2·3)	95 (9·4)	21 (25·9)	<0·0001
30-day mortality, no. (%)	14 (5·3)	320 (31·3)	50 (59·5)	<0·0001

Supplementary Table S6. Characteristics and prognosis of the patients in the external validation cohort and in the phenotypes as predicted by the model in this cohort. Only the variables considered in the probabilistic model are included, as not all variables are available in this cohort.

	All cohort (n=2185)	Phenotype A (n=323)	Phenotype B (n=1757)	Phenotype C (n=105)	P value
DEMOGRAPHICS					
Age, mean (SD), y	67·61 (16·75)	51·05 (17·15)	69·89 (14·83)	80·24 (12·85)	<0·0001
Male gender, no. (%)	1203 (55·1)	133 (41·2)	1013 (57·7)	57 (54·3)	<0·0001
COMORBILITIES					
Chronic lung disease, no. (%)	177 (8·1)	14 (4·3)	142 (8·1)	21 (20·0)	<0·0001
Obesity (BMI>30), no. (%)	356 (16·3)	23 (7·1)	305 (17·4)	28 (26·7)	<0·0001
INFECTION DATA AT ADMISSION					
INFLAMMATION					
White blood cells, mean (SD), $x10^3$ cells/µL	7·35 (4·51)	8·14 (4·97)	6·97 (3·49)	11·27 (11·15)	<0·0001
Neutrophils, mean (SD), $x10^3$ cells/µL	5·17 (3·01)	4·36 (2·75)	5·18 (2·84)	7·54 (4·88)	<0·0001
C reactive protein, mean (SD), mg/L	108 (87)	59 (67)	116 (87)	120 (95)	<0·0001
CARDIOVASCULAR					
Diastolic blood pressure, mean (SD), mmHg	74·11 (12·47)	75·27 (12·46)	74·34 (12·26)	66·75 (13·77)	<0·0001
RESPIRATORY TRACT					
Oxygen saturation (room air, pulse oximetry), mean (SD), %	92·44 (5·59)	96·92 (1·56)	91·80 (5·08)	89·35 (11·59)	<0·0001
Lung infiltrate on chest radiography					<0·0001
No infiltrate, no. (%)	452 (20·7)	169 (52·3)	257 (14·6)	26 (24·8)	
Unilateral, no. (%)	414 (18·9)	79 (24·5)	317 (18·0)	18 (17·1)	
Bilateral, no. (%)	1319 (60·4)	75 (23·2)	1183 (67·3)	61 (58·1)	
RENAL/HYDROELECTROLITIC					
Creatinine, mean (SD), mg/dL	0·99 (0·80)	0·82 (0·48)	0·91 (0·41)	2·86 (2·49)	<0·0001
Sodium, mean (SD), mEq/L	137·98 (4·71)	139·30 (3·64)	137·65 (4·56)	139·42 (8·01)	<0·0001
Potassium, mean (SD), mEq/L	3·99 (0·52)	4·01 (0·46)	3·95 (0·50)	4·50 (0·79)	<0·0001
HEMATOLOGICAL					
Haematocrit, mean (SD), %	42·73 (5·11)	43·17 (4·48)	42·94 (4·92)	37·89 (7·27)	<0·0001
International normalised ratio, mean (SD)	1·22 (0·83)	1·08 (0·30)	1·13 (0·42)	3·17 (2·66)	<0·0001
Blood glucose, mean (SD), mg/dL	119·97 (53·75)	102·94 (27·31)	120·84 (49·79)	157·70 (118·95)	<0·0001
COMPLICATIONS AND PROGNOSIS					
Acute respiratory distress syndrome (ARDS), no (%)	204 (9·4)	6 (1·9)	182 (10·4)	16 (15·2)	<0·0001
Admission to ICU, no (%)	141 (6·5)	9 (2·8)	127 (7·3)	5 (4·8)	0·0089
In-hospital mortality, no (%)	483 (22·1·)	12 (3·7)	417 (23·7·)	54 (51·4)	<0·0001

Supplementary Table S7. Mortality rates in the different cohorts and in the phenotypes. P values were obtained for the comparison of mortality among the phenotypes.

COHORT	Full cohort No. dead/No. in the cohort (%)	Phenotype A No. dead/No. in the phenotype (%)	Phenotype B No. dead/No. in the phenotype (%)	Phenotype C No. dead/No. in the phenotype (%)	P value
Derivation cohort (cluster analysis)	729/2667 (27·3)	13/516 (2·5)	597/1955 (30·5)	119/196 (60·7)	<0·0001
Internal Validation cohort (cluster analysis)	384/1368 (28·1)	6/233 (2·6)	316/1019 (31·0)	62/116 (53·4)	<0·0001
Internal Validation cohort (phenotypes assigned by the probabilistic model)	384/1368 (28·1)	14/263 (5·3)	320/1021 (31·3)	50/84 (59·5)	<0·0001
External Validation cohort (phenotypes assigned by the probabilistic model)	483/2185 (22·1)	12/323 (3·7)	417/1757 (23·7)	54/105 (51·4)	<0·0001

Supplementary Table S8. Association of the phenotypes with 30-day mortality in the derivation cohort, according to age and oxygen saturation.

Stratification variable		Phenotype	30-day mortality No. dead/No. in the phenotype (%)	HR (95% CI)	P
Age	≤60 years	A	0/300 (0)	Reference	
		B	57/530 (10·7)	34·0 (4·7–245·9)	<0·0001
		C	6/15 (40·0)	153·3 (18·4–1274·0)	<0·0001
	>60 years	A	13/216 (6·0)	Reference	
		B	540/1425 (37·9)	7·5 (4·4–13·1)	<0·0001
		C	113/181 (62·4)	16·4 (9·2–29·2)	<0·0001
Oxygen saturation at admission (room air)	>95%	A	5/388 (1·3)	Reference	
		B	143/629 (22·7)	19·6 (8·0–47·8)	<0·0001
		C	24/53 (45·3)	48·39 (18·5–126·9)	<0·0001
	≤95%	A	8/128 (6·2)	Reference	
		B	454/1326 (34·2)	6·4 (3·2–13·0)	<0·0001
		C	95/143 (66·4)	17·4 (8·5–35·9)	<0·0001

4. SUPPLEMENTARY FIGURES

Figure S1. Databases used and procedures performed.

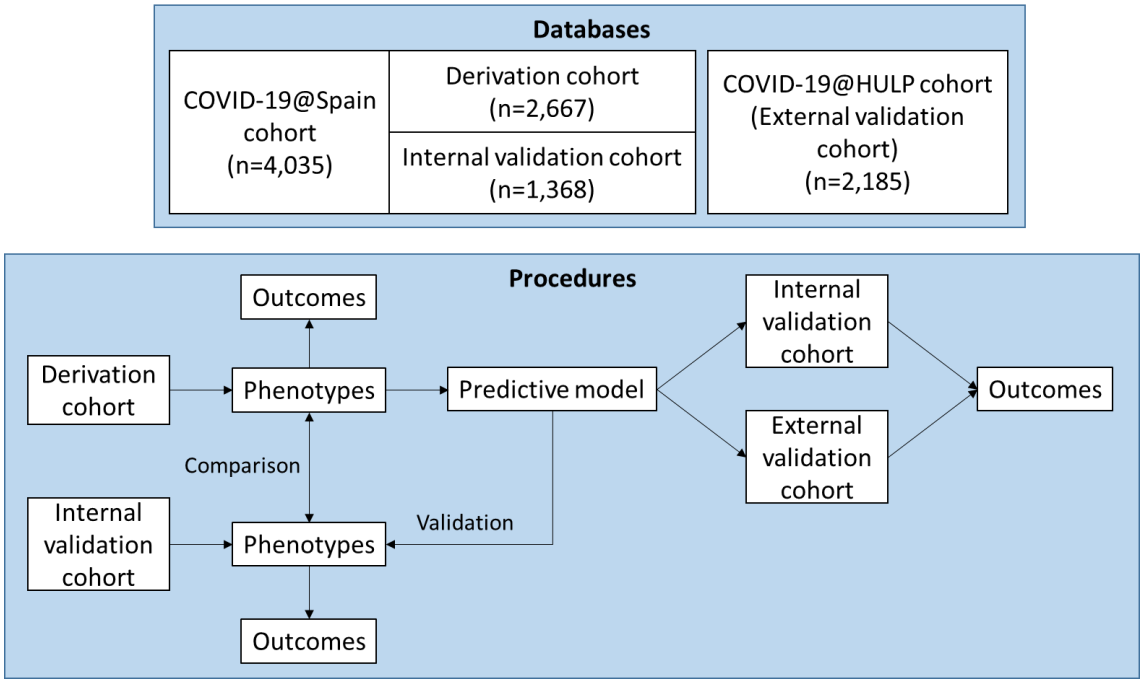


Figure S2. Chord diagram of the distribution of groups of variables into phenotypes in the internal validation cohort.

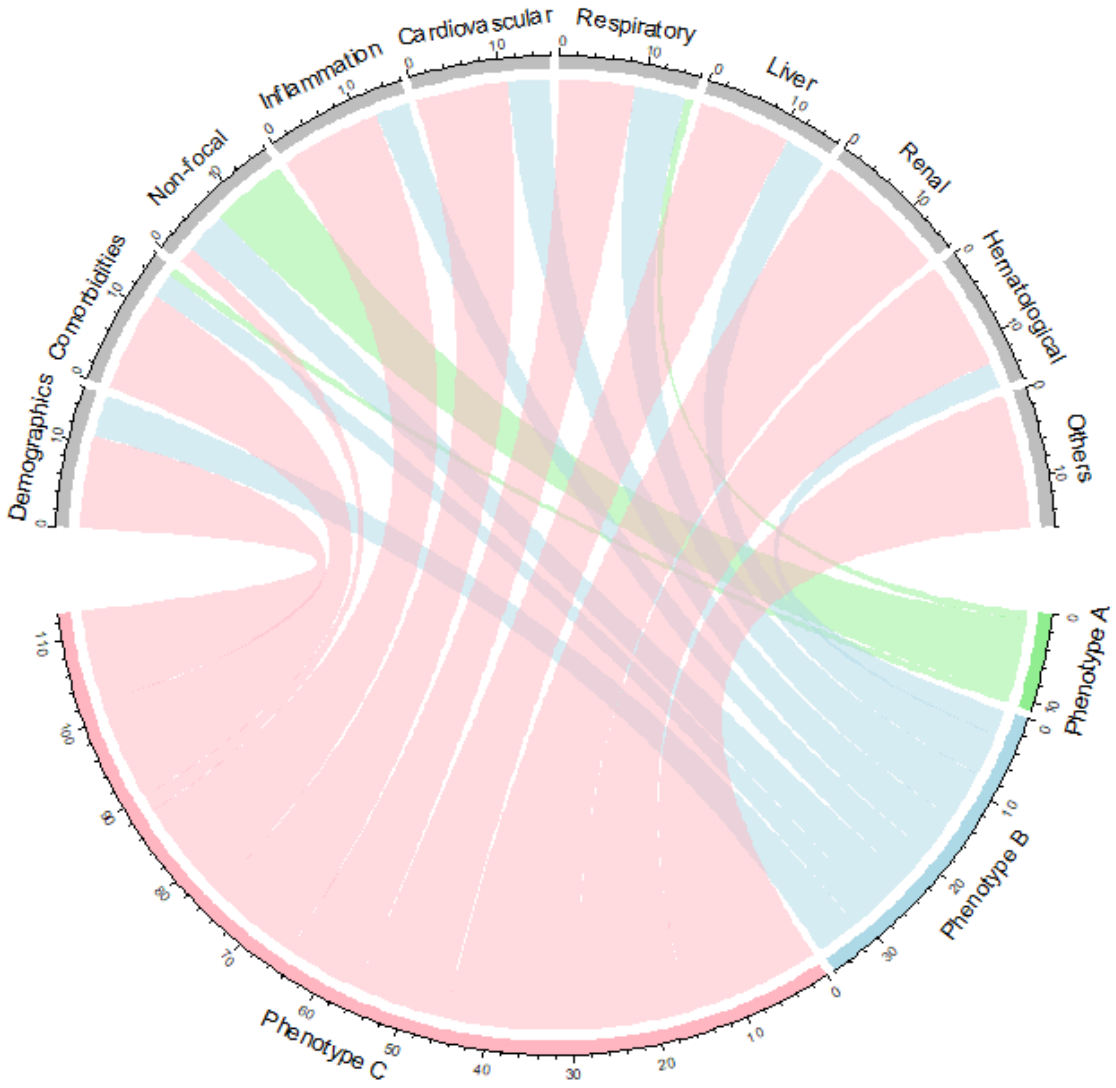


Figure S3. Heatmap of continuous variables according to phenotypes in the internal validation cohort.

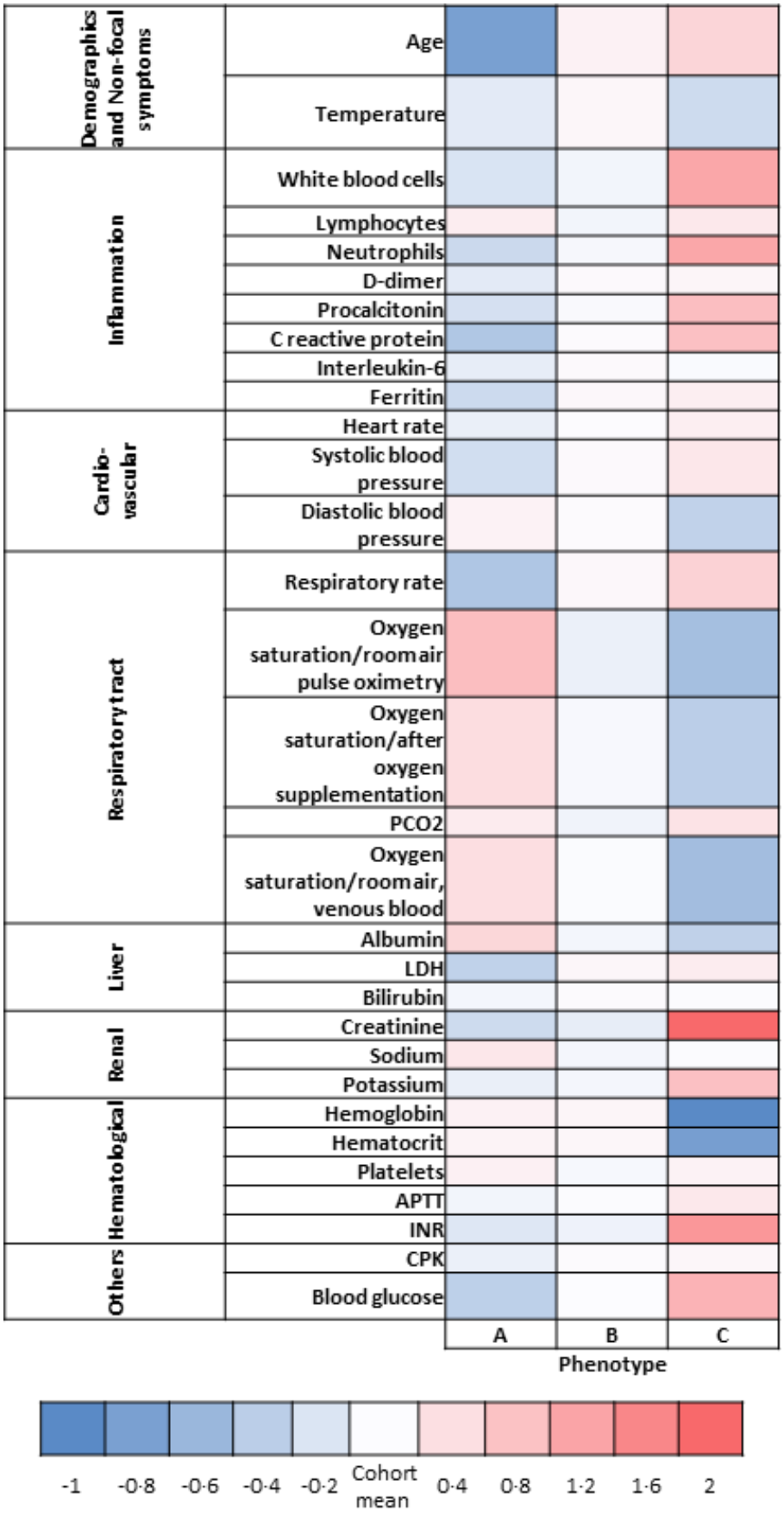
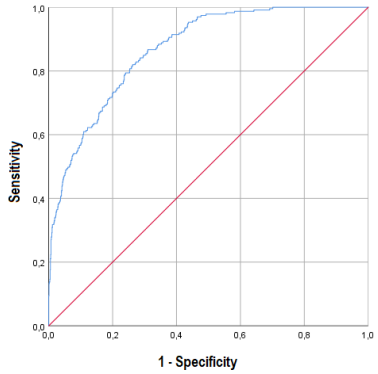
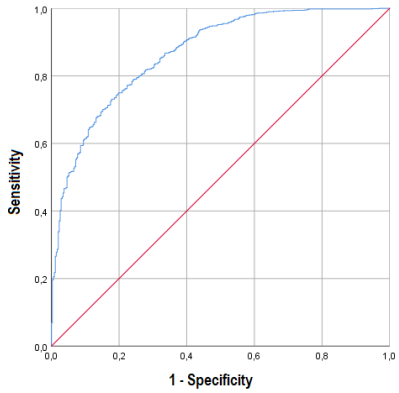


Figure S4. Receiver operating curves for the multinomial regression models for predicting phenotypes A, B and C.

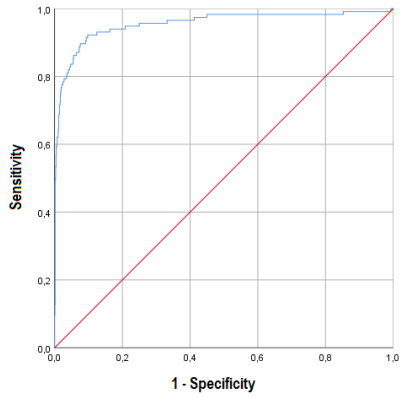
Phenotype A Area under the ROC curve: 0·86; 95% CI 0·84 – 0·89



Phenotype B Area under the ROC curve 0·86; 95% CI 0·84 – 0·88



Phenotype C Area under the ROC curve 0·95; 95% CI 0·93 – 0·98



5. MEMBERS OF THE REIPI-SEIMC COVID-19 AND COVID@HULP GROUPS

REIPI-SEIMC Study Group

Fundación SEIMC-GESIDA:
Aznar Muñoz, Esther
Gil Divasson, Pedro
González Muñiz, Patricia
Muñoz Aguirre, Clara

Hospital Universitario Virgen Macarena:
Retamar, Pilar
Valiente, Adoración
López-Cortés, Luis E.
Sojo-Dorado, Jesús
Bravo-Ferrer, José
Salamanca, Elena
Palacios-Baena, Zaira R.
Pérez-Palacios, Patricia
Gandullo-Moro, María
Ruíz-Hueso, Rocío
Moya-González, Natalia
Valido-Morales, Agustín
Pavón-Masa, María.

Hospital Universitario La Paz:
Díaz Menéndez, Marta
De la Calle Prieto, Fernando
Arsuaga Vicente, Marta
Trigo Esteban, Elena
De Miguel Buckley, Rosa
Cadiñanos Loidi, Julen
Busca Arenzana, Carmen
Mican Rivera, Rafael
Mora Rillo, Marta
Loeches Yagüe, Belén
Bernardino de la Serna, José Ignacio
García Rodríguez, Julio
Montejano Sánchez, Rocío
Diaz Pollan, Beatriz

Hospital Universitario Gregorio Marañón
López, Juan Carlos
Ramírez-Schacke, Margarita
Gutiérrez, Isabel
Tejerina, Francisco
Aldámiz-Echevarría, Teresa
Díez, Cristina
Fanciulli, Chiara
Pérez-Latorre, Leire
Parras, Francisco
Catalán, Pilar
García-Leoni, María E
Pérez-Tamayo, Isabel
Puente, Luis
Cedeño, Jamil

Hospital Infanta Leonor
Such-Diaz, Ana
Álvaro-Alonso, Elena
Izquierdo-García, Elsa
Torres-Macho, Juan
Cuevas, Guillermo
Notario, Helena
Mestre-Gómez, Beatriz
Jiménez-González de Buitrago, Eva
Fernández-Jiménez, Inés
Tebar-Martínez, Ana Josefa
Brañas, Fátima
Valencia, Jorge
Pérez-Butragueño, Mario
Alvarado, Marta

Hospital Universitari de Bellvitge
Abelenda-Alonso, Gabriela
Ardanuy, Carmen
Bergas, Alba
Cuervo, Guillermo
Domínguez, María Ángeles
Fernández-Huerta, Miguel
Gudiol, Carlota
Lorenzo-Esteller, Laia
Niubó, Jordi
Pérez-Recio, Sandra
Podzamczer, Daniel
Pujol, Miquel
Rombauts, Alexander
Trullen, Núria

Hospital Universitario Virgen del Rocío
Cisneros, José Miguel
Amodeo, Cristina
Camacho, Pedro
Espinosa, Nuria
García-Gutiérrez, Manuel
Jara-Palomares, Luis
González-León, Rocío
Molina, José
Nieto Martín, María Dolores
Paniagua, María
Poyato, Manuel
Rodríguez-Villodres, Ángel
Ruiz de Azua, Zaida
Salamanca, Celia

Complejo Hospitalario Virgen de la Salud
Sepúlveda Berrocal, Mª Antonia
Yera Bergua, Carmen
Toledano Sierra, Pilar
Cano Llorente, Verónica
Zafar Iqubal-Mirza, Sadaf
Muñiz, Gema
Martín Pérez, Inmaculada
Mozas Moriñigo, Helena
Alguacil, Ana
García Butenegro, María Paz

Hospital Universitario Rafael Méndez
Peláez Ballesta, Ana Isabel
Morcillo Rodríguez, Elena

Hospital Universitario de Cruces
Goikoetxea Agirre, Josune
Blanco Vidal, María José
Nieto Arana, Javier
del Álamo Martínez de Lagos, Mikel

Hospital de Melilla
Pérez Hernández, Isabel A.
Pérez Zapata, Inés

Hospital San Eloy de Barakaldo
Silvariño Fernández, Rafael
Ugalde Espiñeira, Jon

Hospital Universitario Central de Asturias
Rivas-Carmenado, María
Suárez Pérez, Lucia
Suárez Diaz, Silvia
Yllera Gutiérrez, Carmen

Hospital General Universitario de Alicante
Boix, Vicente
Díez Martínez, Marcos
Carreres Candela, Melissa

Hospital Virgen de la Victoria
Gómez-Ayerbe, Cristina
Sánchez-Lora, Javier
Velasco Garrido, José Luis
López-Jodar, María
Santos González, Jesús

Hospital Universitario Puerto Real
Ruiz Aragón, Jesús
Virto Peña, Ianire

EOXI Pontevedra e Salnés
Alende Castro, Vanessa
Sande Llovo, Diana

Hospital de Figueres
Vega Molpeceres, Sonia
Pons Viñas, Estel

Hospital Sant Jaume de Calella
del Río Pérez, Oscar
Valero Rovira, Silvia

Hospital del Mar
Villar-García, Judit
Gómez-Junyent, Joan
Cánepa, María Cecilia
Castañeda Espinosa, Silvia
Letang, Emilio
Arenas-Miras, Mª del Mar
Gómez-Zorrilla, Silvia
Sánchez Martínez, Francesca
Lerma-Chippirraz, Elisabet

Hospital Clínico Universitario Virgen de la Arrixaca- IMIB

García Vázquez, Elisa
Moral Escudero, Encarnación
Roura Piloto, Aychel Elena

Hospital de Can Misses
García Almodóvar, Esther

Hospital de Sagunto
Sáez Barberá, Carmen
Karroud, Zineb

Hospital Clínico San Cecilio
Hernández Quero, José
Vinuesa García, David
García Fogeda, José Luis
Peregrina, José Antonio

Hospital Universitario Príncipe de Asturias
Novella Mena, María
Hernández Gutiérrez, Cristina
Sanz Moreno, José
Pérez Tanoira, Ramón
Navarro López, Jorge
Balsa Vázquez, Javier
Gutiérrez García, Aida
Arranz Caso, Alberto
Cuadros González, Juan
Álvarez de Mon Soto, Melchor

Parc Sanitari Sant Joan de Déu
Díaz De Brito Fernández, Vicente Ferrer
Sanmarti Vilamala, Montserrat
Gabarrell Pascuet, Aina
Molina Morant, Daniel
España Cueto, Sergio
Cámara Fernández, Jonathan
Sabater Gil, Albert
Muñoz López, Laura

Hospital Nuestra Señora de Gracia
Jorge García, Ruth
Molina Torres, Nora

HC Marbella Internacional Hospital
Sempere Alcocer, Marco Antonio
De Castro Vega, Francisco Javier

Hospital Universitario La Princesa
De los Santos Gil, Ignacio
García-Fraile, Lucio
Sampedro Núñez, Miguel
Barrios Blandino, Ana
Rodríguez Franco, Carlos
Useros Brañas, Daniel
Villa Martí, Almudena
Oliver Ortega, Javier
Costanza Espiño Álvarez, Alexia
Sanz Sanz, Jesús

Hospital Josep Trueta
Rexach Fumaña, María
Policarpo Torres, Guillem
Ortega Montoliu, Meritxell

Hospital Dos de Maig – Consorcio Sanitari Integral
Sala Jofre, Clara
Casas Rodríguez, Susana

Hospital Arnau de Vilanova-Lliria
Tortajada Alamilla, Cecilia
Oltra, Carmina

Hospital General Universitario de Elche
Masiá Canuto, Mar
Gutiérrez Rodero, Félix

Hospital Clínico Universitario de Valencia
Oltra Sempere, Mª Rosa
Vela Berna, Sara

Complejo Asistencial de Ávila
Pedromingo Kus, Miguel
Garcinuño, María Ángeles
De la Vega, Alexandra
Pérez Pinto, Sergio

Hospital Comarcal de Alcañiz
Hernández Machín, Pilar
Alastrué Violeta, Alba

Hospital Universitario Marqués de Valdecilla
Fariñas Álvarez, María Carmen
González Rico, Claudia
Arnaiz de las Revillas, Francisco
Calvo, Jorge
Gozalo, Mónica

Hospital Quirón-Salud de Torrevieja
Mora Gómez, Francisco

Hospital Universitario Miguel Servet
Milagro Beamonte, Ana
Latorre-Millán, Miriam
Rezusta López, Antonio
Martínez Sapiña, Ana

Hospital de Barcelona SCIAS
Meije, Yolanda
Ribera Puig, Alba
Ortega Enciso, Lucía
Sanz Salvador, Xavier

Fundación Hospital Universitario Alcorcón
Losa García, Juan Emilio
Velasco Arribas, María

Hospital Álvaro Cunqueiro
Pérez-Rodríguez, M. Teresa
Pérez González, Alexandre

Complejo Asistencial Universitario de Salamanca
Belhassen-García, Moncef
Rodríguez-Alonso, Beatriz
López-Bernus, Amparo
Carbonell, Cristina

Hospital Universitario Severo Ochoa
Torres Perea, Rafael
Cantón De Seoane, Juan
Alonso, Blanca
Kamal, Sara Lidia
Cajuela, Lucia
Roa, David
Cervero, Miguel
Oreja, Alberto
Avilés, Juan Pablo
Martín, Lidia

Hospital CIMA-Sanitas
Pelegrín Senent, Iván
Rouco Esteves Marques, Rosana

Hospital HLA Inmaculada
Parra Ruiz, Jorge
Ramos Sesma, Violeta

Hospital Universitario Rio Hortega
Abadia Otero, Jésica

Hospital de Guadalajara
Salillas Hernando, Juan
Torres Sánchez del Arco, Robert
Torralba González de Suso, Miguel
Serrano Martínez, Alberto
Gilaberte Reyzábal, Sergio
Pacheco Martínez-Atienza, Marina
Liébana Gómez, Mónica
Fernández Rodríguez, Sara
Varela Plaza, Álvaro
Calvo Sánchez, Henar

Hospital Universitario Infanta Sofía
Martínez Martín, Patricia
González- Ruano, Patricia
Malmierca Corral, Eduardo
Rábago Lorite, Isabel
Pérez-Monte Mínguez, Beatriz

Hospital Comarcal de Blanes
García Flores, Ángeles
Comas Casanova, Pere

Hospital Universitari de Tarragona Joan XXIII
Sirisi, Merce
Rojas, Richard

Hospital Universitario Basurto
Díaz de Tuesta del Arco, José Luis
Figueroa Cerón, Ruth
González Sarria, Ander

Hospital Universitario de Canarias
Alemán Valls, Remedios
Alonso Socas, María del Mar

Hospital Universitario de Gran Canaria Dr. Negrín
Sanz Peláez, Oscar
Mohamed Ramírez, Karim

Hospital Son Espases
Riera Jaume, Melchor
Vilchez, Helem Haydee
Albertí, Francesc
Cañabate, Ana Isabel

Hospital Universitario de Móstoles
Moreno Cuerda, Víctor J
Álvarez Kaelis, Silvia
Álvarez Zapatero, Beatriz
García García, Alejandro
Isaba Ares, Elena
Morcate Fernández, Covadonga
Pérez Rodríguez, Andrea

Complejo Hospitalario Universitario A Coruña
Ramos Merino, Lucía
Castelo Corral, Laura
Rodríguez Mahía, María
González Bardanca, Mónica
Sánchez Vidal, Efrén
Míguez Rey, Enrique

Hospital Costa del Sol
Correa Ruiz, Ana
García de Lomas Guerrero, José Mª

Hospital Clínico Universitario Lozano Blesa
Daniel López, Daniel
Marinas, Rebeca
Morando, Marta

Hospital Mutua de Terrassa
Gómez García, Lucía
Boix Palop, Lucia
Dietl Gómez-Luengo, Beatriz

Hospital de la Plana
Pedrola Gorrea, Iris
Blasco Claramunt, Amparo

Hospital Virgen de la Concha - Complejo Asistencial de Zamora
López Mestanza, Cristina
Fraile Villarejo, Esther

Complejo Hospitalario Universitario Insular Materno-Infantil
Jaén Sánchez, Nieves
Orihuela Martín, Jorge

Hospital de la Marina Baixa
Algado Rabasa, José Tomas
Garijo Saiz, Ana María
Amador Prous, Concepción

Hospital Universitario y Politécnico La Fe
Salavert Lletí, Miguel

Hospital Universitario del Vinalopó
Hernández Belmonte, Adriana
Martínez Goñi, Raquel

Hospital Parc Taulí de Sabadell
Navarro Vilasaró, Marta
Calzado Isbert, Sonia
Cervantes García, Manuel
Gomila Grange, Aina
Gasch Blasi, Oriol
Machado Sicilia, María Luisa
Van den Eynde Otero, Eva
Falgueras López, Luis
Navarro Sáez, María del Carmen

Hospital Clinic de Barcelona
Martínez, Esteban
Marcos, Mª Ángeles
Mosquera, Mar
Blanco, José Luis
Laguno, Montserrat
Rojas, Jhon
González-Cordón, Ana
Inciarte, Alexy
Torres, Berta
De la Mora, Lorena
Soriano, Alex

Hospital Universitario de la Ribera
Martínez Macias, Olalla
Pérez Doñate, Virginia

Fundación Jiménez Díaz
Cabello Úbeda, Alfonso
Carrasco Antón, Nerea
Álvarez Álvarez, Beatriz
Petkova Saiz, Elizabet
Górgolas Hernández-Mora, Miguel
Prieto Pérez, Laura
Carrillo Acosta, Irene
Heili Frades, Sara
Villar Álvarez, Felipe
Fernández Roblas, Ricardo
Sánchez Pernaute, Olga

Hospital Clínico Universitario de Valladolid
Fernández Espinilla, Virginia
Castrodeza Sanz, José Javier
Dueñas Gutiérrez, Carlos Jesús

Hospital Clínico San Carlos
González-Romo, Fernando
Merino Amador, Paloma
Rueda López, Alba
Martínez Jordán, Jorge
Medrano Pardo, Sara
Díaz de la Torre, Irene
Posada Franco, Yolanda
Delgado-Iribarren, Alberto

Hospital Santa Creu i Sant Pau
López-Contreras González, Joaquín
Pascual Alonso, Pablo
Pomar Solchaga, Virginia
Rabella García, Nuria
Benito Hernández, Natividad
Domingo Pedrol, Pere
Bonfill Cosp, Xavier
Padrós Selma, Rafael
Puig Campmany, Mireia
Mancebo Cortés, Jordi
Gurguí Ferrer, Mercè

Clínica Universitaria de Navarra - Campus Madrid
Íñigo Pestaña, Melania
Pérez García, Alejandra

Hospital Son Llatzer
Sorní Moreno, Patricia
Izko Gartzia, Nora

Hospital General de la Defensa Gómez Ulla
Membrillo de Novales, Francisco Javier
Simón Sacristán, María
Zamora Cintas, Maribel
Martínez Martínez, Yolanda
Estébanez Muñoz, Miriam
Ramírez-Olivencia, Germán
Herrero Mendoza, María Dolores
De Dios García, Begoña
Mata Forte, Tatiana
Rodríguez Fernández, José María

Hospital Universitario de Álava
Sáez de Adana Arróniz, Ester
Portu Zapirain, Joseba
Gainzarain Arana, Juan Carlos
Ortiz de Zárate Ibarra, Zuriñe
Moran Rodríguez, Miguel Ángel
Canut Blasco, Andrés
Hernáez Crespo, Silvia
Sanjosé Muñiz, Irene

Molina Iturritza, Estíbaliz
Ganchegui Aguirre, Maite
Urrestarazu Larrañaga, Miren

Hospital Santos Reyes
De la Higuera Arranz, Carmen
Álvarez Padín, Pilar

Hospital Dr. José Molina Orosa
Iglesias Llorente, Laura
Román Bernal, Berta

Hospital Vall d´Hebrón
Sánchez Montalvá, Adrián
Espinosa Pereiro, Juan
Almirante, Benito
Miarons, Marta
Sellarés, Júlia
Larrosa, María
Villamarín, Miguel
Fernández, Nuria
Salvador, Fernando
Bosch-Nicolau, Pau

Hospital Universitario Rey Juan Carlos
Pérez-Jorge Peremarch, Conchita
Resino Foz, Elena
Espigares Correa, Andrea
Álvarez de Espejo Montiel, Teresa
Navas Clemente, Iván
Quijano Contreras, María Isabel
Nieto Fernández del Campo, Luis Alberto
Jiménez Álvarez, Guillermo

Complejo Hospitalario Universitario Santa Lucía
Guillamón Sánchez, Mercedes
García García, Josefina

Hospital Santa Bárbara
Muñoz Hornero, Constanza
Cosmen Sánchez, Ana

Complejo Hospitalario Universitario de Ferrol
Mariño Callejo, Ana
Valcarce Pardeiro, Nieves

Hospital de l'Esperit Sant
Smithson Amat, Alex
Chico Chumillas, Cristina

Hospital Universitario los Arcos del Mar Menor
Sánchez Serrano, Adriana
Piñar Cabezos, Diana

Hospital HLA Universitario Moncloa
Jiménez Martínez, Isabel
Estrada Fernández, Guillermo
Lorén Vargas, María
Parra Arribas, Nuria
Martínez Cilleros, Carmen
Villasante de la Puente, Aránzazu
García Delange, Teresa
Ruiz Rodríguez, María José
Robledo del Prado, Marta
Abad Almendro, Juan Carlos

Hospital Virgen del Puerto
Muñoz del Rey, José Román
Jiménez Álvaro, Montaña

Hospital Marina Salud de Dénia
Coy Coy, Javier
Poquet Catala, Inmaculada

Hospital Universitario de Jerez
Santos Peña, Marta
Mora Delgado, Juan

Hospital Reina Sofía de Tudela
Manso Gómez, Tamara
Rubio Obanos, Teresa

Hospital Clínico Universitario de Santiago de Compostela
Barbeito Castiñeiras, Gema
Domínguez Santalla, María Jesús

Hospital Universitario del Henares
Mao Martín, Laura
Adalid Moll, María
Díaz Luperena, Javier
Ruiz Grinspan, Martín Sebastián
Barrós González, Raquel
Herrera Pacheco, Lourdes
Martínez Avilés, Rocío
Rodrigo González, Sara
Rodríguez Leal, Cristóbal Manuel

Hospital Universitario Lucus Augusti
Romay Lema, Eva María
Suárez Gil, Roi

Hospital de Donostia
Bustinduy Odriozola, Maria Jesús
Marimón Ortiz de Zárate, José María
Vidaur Tello, Loreto
Kortajarena Urkola, Xabier

Hospital de Urduliz Alfredo Espinosa
Arriola Martínez, Paula
Lartategi Iraurgi, Alazne

Hospital de Mendaro
Álvarez de Castro, Maria
Martínez Mateu, Cintia María

Hospital Juan Ramón Jiménez
Rodríguez Gómez, Francisco
Asschert Agüero, Isabel

Hospital de Tortosa Virgen de la Cinta
Chamarro Martí, Elena
Franch Llasat, Diego

Hospital Riotinto
Zakariya-Yousef Breval, Ismail
Rico Rodríguez, Marta

Hospital Vega Baja
Martínez López, Belén
García-López, María

Hospital Puerta de Hierro
Fernández Cruz, Ana
Calderón Parra, Jorge
Ramos Martínez, Antonio
Múñez Rubio, Elena
Vázquez Comendador, José Manuel
Diego Yagüe, Itziar
Expósito Palomo, Esther
Díaz de Santiago, Alberto
De la Fuente Moral, Sara
Pintos Pascual, Ilduara

Hospital Universitario de Getafe
Álvarez Franco, Raquel
Fernández de Orueta, Lucía
Vates Gómez, Roberto
Cardona Arias, Andrés Felipe
Marguenda Contreras, Pablo
Gaspar Alonso-Vega, Gabriel
Aranda Rife, Elena María
Martínez Cifre, Blanca
Roger Zapata, Daniel
Martín Rubio, Irene

Hospital General de la Palma
Barbosa Ventura, André
Piñero, Iván

Hospital El Bierzo
Bahamonde Carrasco, Alberto
Martínez Vidal, Ana

Fundación Hospital de Calahorra
Talavera García, Eva
Mendoza Roy, Paula

Hospital Alto Deba
Urrutia Losada, Ainhoa
Arteche Eguizabal, Lorea

Hospital Universitario San Juan de Alicante
Delgado Sánchez, Elisabet
Bañón Escandell, Sara

Hospital de Guadarrama
Caro Bragado, Sarah
Domínguez de Pablos, Gema

Hospital Universitario de Jaén
Herrero Rodríguez, Carmen
Liébana Martos, Carmen

Hospital de Mataró
Force Sanmartín, Luis
Aranega, Raquel

Hospital de Palamós
Mera Fidalgo, Arantzazu
Hortos Alsina, Miquel

Hospital Universitario de Valme
Merchante Gutiérrez, Nicolas
León Jiménez, Eva María

Clínica Universitaria de Navarra - Campus Navarra
Del Pozo León, José Luís

Hospital Clínica Benidorm
Serralta Buades, Josefa
Cabrera Tejada, Ginger Giorgiana

Hospital Doce de Octubre
Fernández-Ruiz, Mario
Aguado, José María
Maestro de la Calle, Guillermo

Hospital Universitario Ramón y Cajal
Vizcarra, Pilar
Rodriguez Dominguez, Mario José
Gioia, Francesca
Del Campo, Santos
Cantón Moreno, Rafael
Martín Dávila, Pilar
Casado, José L.

Hospital Universitario San Pedro
Oteo Revuelta José, Antonio
Santibáñez Sáenz, Paula
Cervera Acedo, Cristina
Ruiz Martínez, Carlos
Blanco Ramos, José R.
Azcona Gutiérrez, José M.
García García, Concepción
Alba Fernández, Jorge
Ibarra Cucalón, Valvanera
San Franco, Mercedes
Metola Sacristán, Luis

Hospital Quirón A Coruña
Meijide Míguez, Héctor
Gredilla Zubiría, Íñigo

HM Sanchinarro
Menéndez, Justo
Villares Fernández, Paula
Montes Andújar, Lara

Hospital Francesc de Borja
Navarro Batet, Álvaro
Ferrer Santolaria, Anna

Complejo Hospitalario Universitario Nuestra Señora de La Candelaria
Padilla Salazar, María de la Luz
Abella Vázquez, Lucy
Hayek Peraza, Marcelino
García Pardo, Antonio
Hernández Carballo, Carolina

Hospital Universitario HM Montepríncipe
Ruiz Fernández, Andrés Javier
Barrio López, Isabel

Hospital Universitario HM Puerta del Sur
Martakoush Alí

Hospital Universitario HM Torrelodones
Rojas-Vieyra, Agustín

Hospital Universitario HM Madrid
García Calvo, Sonia
Villarreal García-Lomas, Mercedes

Hospital Don Benito-Villanueva de la Serena
Vizcaíno Callejón, Marta
García García, María Pilar

Hospital de Viladecans
Lérida Urteaga, Ana
Carrasco Fons, Natalia
María Sanjuan, Beatriz
Martín González, Lydia
Sanz Zamudio, Camilo

Centro Nacional de Epidemiología
Alejos, Belén
Moreno, Cristina
Rava, Marta
Iniesta, Carlos
Izquierdo, Rebeca
Suárez-García, Inés
Díaz, Asunción
Ruiz-Alguero, Marta
Hernando, Victoria

COVID@HULP Group

Hospital Universitario La Paz
Frías, Jesús
Ramírez, Elena
Martín-Quirós, Alejandro
Quintana-Díaz, Manuel
Mingorance, Jesús
Arnalich, Francisco
Moreno, Francisco
Figueiras, Juan Carlos
García-Arenzana, Nicolás
Montero-Vega, María Dolores
Romero-Gómez, María Pilar
Toro-Rueda, Carlos
García-Bujalance, Silvia
Ruiz-Carrascosa, Guillermo
Cendejas-Bueno, Emilio
Falces-Romero, Iker
Lázaro-Perona, Fernando
Ruiz-Bastián, Mario
Gutiérrez-Arroyo, Almudena
Girón De Velasco-Sada, Patricia
Dahdouh, Elie
Gómez-Arroyo, Bartolomé
García-Sánchez, Consuelo
Guedez-López, Virginia
Bloise-Sánchez, Iván
Alguacil-Guillén, Marina
Liras-Hernández, Maria Gracia
Sánchez-Castellano, Miguel Angel
García-Clemente, Paloma
González-Donapetry, Patricia
San José-Villar, S
de Pablos-Gómez, Manuela
Gómez-Gil, Rosa
Corcuera-Pindado, Maria Teresa
Rico-Nieto, Alicia
Herrero, Alicia
Prieto-Arribas, Daniel
Oliver-Saez, Paloma
Mora-Corcovado, Roberto
Fernández-Calle, Pilar
Alcaide-Martín, María José
Díaz-Garzón, Jorge
Fernández-Puntero, Belén
Nuñez-Cabetas, Rocío
Crespo-Sánchez, Gema
Rodriguez-Fraga, Olaia
Mendez del Sol, Helena
Duque-Alcorta, Marta
Gomez-Rioja, Rubén
Sanz de Pedro, María
Pascual-García, Lydia
Segovia-Amaro, Marta
Iturzaeta-Sánchez, Jose Manuel
Rodriguez-Gutiérrez, Mercedes
Perez-Garcia Morillón, Amparo
Martinez Gallego, Miguel Angel
Fabre-Estremera, Blanca
Martinez-Chavez , Estefanía
Moreno-Parra , Isabel
Rodriguez-Roca, Neila
Ortiz-Sánchez, Daniel
Simon-Velasco, Manuela
Gabriela-Tomoiu, Ileana
Pizarro-Sanchez, Cristina
Montero-San Martín, Blanca
Qasem-Moreno, Ana Laila
Gómez-López, Marta
Casares Guerrero, Ismael
Buño-Soto, Antonio
Martí de Gracia, Milagros
Parra-Gordo, Luz
Diez-Tascón, Aurea

Ossaba-Vélez, Silvia
Pinilla, Inmaculada
Cuesta, Emilio
Fernández-Velilla, María
Torres, Maria Isabel
Garzón, Gonzalo
Pérez-Blanco, Verónica
Quintás-Viqueira, Almudena
San Juan, Isabel
Cantero-Escribano, José Miguel
Pérez-Romero, César
Castro-Martínez, Mercedes
Hernández-Rivas, Lucía
Pedraz, Teresa
Fernández-Bretón, Eva
García-Vaz, Claudia
Robustillo-Rodela, Ana
Torres Santos-Olmo, Rosario
María
Rivera-Núñez, Angélica
Fernández-Fernández, Ignacio
Noguerol-Gutiérrez, Marina
Martínez-Virto, Ana María
González-Viñolis, Manuel
Cabrera-Gamero, Regina
Mayayo-Alvira, Rosa
Marín-Baselga, Raquel
Lo-Iacono García, Victoria
Lerín-Baratas, Macarena
Romero Gallego-Acho, Paloma
Reche-Martínez, Begoña
Tejada-Sorados, Renzo
Rico-Briñas, Mikel
Deza-Palacios, Ricardo
Fabra-Cadenas, Sara
Arroyo-Rico, Isabel
Ben-Abdellah, Lubna Dani
Labajo-Montero, Laura
Soriano-Arroyo, Rubén
López-Corcuera, Lorena
Calvin-García, Elena
Martínez-Álvarez, Susana
López-Tappero Irazábal, Laura
Pilares-Barco, Martín
González-Peña, Olga
Bejarano-Redondo, Guillermina
Iglesias-Sigüenza, Alberto
Tung-Chen, Yale
Maroun Eid, Charbel
Bravo-Lizcano, Ruth
Silvestre-Niño, Miguel
Perdomo-García, Frank
Alonso-González, Berta
Antón-Huguet, Berta
Arenas-Berenguer, Isabel
Cabré-Verdiell Surribas, Clara
Marqués-González, Francisco
Muñoz del Val, Elena
Ángeles Molina, María
Cancelliere-Fernández, Nataly
Pastor-Yvorra, Sivia
Frade-Pardo, Laura
López-Arévalo, Paloma
García, Isabel
Fernández-Capitán, Carmen
González-Garcia, Juan José
Herrero, Juan
Quesada Simón, María
Angustias
Robles Marhuenda, Angel
Soto Abanedes, Clara
Noblejas Mozo, Ana María
Ramos, Juan Carlos
Jaras Hernandez, María Jesús
Martinez Robles, Elena
Moreno Fernandez, Alberto
Sanchez Purificación, Aquilino
Martin Gutiérrez, Juan Carlos
Martinez Hernández, Pedro Luis
Sancho Bueso, Teresa
Lorenzo Hernández, Alicia
Gutierrez Sancerni, Belén
Salgueiro, Giorgina
Martin Carbonero, Luz
Mostaza, Jose María
Martinez-López, María Angeles
Hontañón, Victor
Menéndez, Araceli
Alvarez Troncoso, Jorge
Castellano, Arancha
Marcelo-Calvo, Cristina
Vives-Beltrán, Ivo
Ramos Ruperto, Luis
Daroca-Bengoa, Germán
Arcos Rueda, María
Vasquez-Manau, Julia
Fernández Cidón, Pelayo
Rosario Herrero Gil, Carmen
Palmier Peláez, Esmeralda
Untoria Tabares, Yeray
Lahoz, Carlos
Estirado, Eva
Hernández, Clara
Garcia-Iglesias, Francisca
Monteoliva, Enrique
Martínez, Mónica
Varas, Marta
González Alegre, Teresa
Valencia, Maria Eulalia
Moreno, Victoria
Montes, Maria Luisa
Alcolea-Batres, Sergio
Cabanillas-Martín, Juan José
Carpio-Segura, Carlos
Casitas-Mateo, Raquel
Fernández-Bujarrabal
Villoslada, Jaime
Fernández-Navarro, Isabel
Fernández-Lahera, Juan
García-Quero, Cristina
Hidalgo-Sánchez, María
Galera-Martínez, Raúl
García-Río, Francisco
Gómez-Carrera, Luis
Gómez-Mendieta, María
Antonia
Mangas-Moro, Alberto
Martínez-Cerón, Elisabet
Martínez-Redondo, María
Martínez-Abad, Yolanda
Martínez-Verdasco, Antonio
Plaza-Moreno, Cristina
Quirós-Fernández Sarai
Romera-Cano, Delia
Romero-Ribate, David
Sánchez-Sánchez, Begoña
Santiago-Recuerda, Ana
Villasante Fernández-Montes,
Carlos
Zamarrón de Lucas, Ester
Arnalich-Montiel, Victoria
Mariscal-Aguilar, Pablo
Falcone, Adalgisa
Laorden-Escudero, Daniel
Prados Sánchez, María
Concepción
Álvarez-Sala Walther, Rodolfo
García, Andony
Arévalo, Cristina
Gutiérrez, Carola
Yus, Santiago
Asensio, Maria José
Sánchez, Manolo
Añón, Jose Manuel
Manzanares, Jesús
García de Lorenzo, Abelardo
Perales, Eva
Civantos, Belén
Cachafeiro, Lucía
Agrifoglio, Alexander
Estébanez, Belén
Flores, Eva
Hernández, Mónica
Millán, Pablo
Rodríguez, Montserrat
Nanwani, Kapil
Arizcun, Beatriz
Pérez-Costa, Elena
Rodríguez-Álvarez, Diego
Sánchez-Martín, María
Quesada, Úrsula
Román-Hernández, Carmen
Dorao, Paloma
Álvarez-Rojas, Elena
Menéndez, Juan José
Verdú, Cristina
Gómez-Zamora, Ana
Schüffelmann, Cristina
Calderón-Llopis, Belén
Laplaza-González, María
Río-García, Miguel
Amores-Hernández, Irene
Rodríguez-Rubio, Miguel
de la Oliva Pedro
Ruiz, Jose
Rosillo, Sandra
González, Oscar
Iniesta, Angel
Ponz, Ines
Muñoz-Ramón, José María
Hernández-Gancedo, María
Uña Orejón, Carmen R.
Sanabria-Carretero, Pascual
Moreno Gómez-Limón, Isidro
Seiz-Martinez, Alverio
Guasch-Arévalo, Emilia
Martín-Carrasco, Cristina
Alvar, Elena
Serrá, Lucía
Iannuccelli, Fabricio
Latorre, Julieta

Casares, Sandra
Valbuena, Isabel
Díaz Díez Picazo, Luis
Rodríguez Roca, Cristina
Cervera, Omar
García de las Heras, Esteban
Durán, Pilar
Castro, Carmen
Manrique de Lara, Carlos
Veganzones, Javier
López-Tofiño, Araceli
Fernandez-Cerezo, Estefanía
Zurita, Sergio
López-Martinez, Mercedes
Prim, Teresa
Alvárez del Vayo, Julía
Alcaraz, Gabriela
Castro, Luis
Yagüe, Julio
Díaz-Carrasco, Sofía
González-Pizarro, Patricio
Montero, Ana
Sagra, Francisco Javier
Suárez, Alejandro
Díez-Porres, Leyre
Varela-Cerdeira, María
Alonso-Babarro, Alberto
Abellán Martínez, Francisco
Alonso-Eiras, Jorge Ignacio
Álvarez Brandt, Alejandra
Archinà, Martina
Arribas-Terradillos, Silvia
Baselga-Puente, Trinidad
Barco Núñez, Pilar
Barrera-López, Natalia
Guadalupe
Barrera-López, Lorena
Bartrina-Tarrio, Andres
Bassani, Gemma
Betancort De la Torre, Paula
Blanco-Bartolomé, Irene
Blasco-Andres, Celia
Brieba-Plata, Lucía
Cadenas-Gota, Fernando
Carrera-Vázquez, Paloma
Cascajares-Sanz, Carlota
Catino, Arianna
Cavallé-Pulla, Raquel
Ceniza-Pena, Daniel
Conde-Alonso, Ylenia María
Currás-Sánchez, Laura
Daltro-Lage, Marcelo
Esteban-Romero, Ana
Fernández Vidal, María Luisa
Ferrer Ortiz, Inés
de la Fuente Regaño, Lydia
Galindo-Ballesteros, Pablo
Garcia-Bellido Ruiz, Sara
García-Mochales Fortún, Carlos
Gómez-Ballesteros, Teresa
Gómez-Domínguez, Cecilia
González-Aguado, Nelsa
González-García, Sofía
Jorge Guisández Martín
Hernández-Liebo, Paula
Alejandra
Hernando Nieto, Raquel
Llorente-Cortijo, Irene María
Marín-García, Antonio
López-Pirez, Pilar
Mejuto-Illade, Lucía
Palma, Marco
Peña-Hidalgo, Adrian
Platero-Dueñas, Lucía
Pujol-Pocull, David
Ramírez-Verdyguer, Miguel
Redondo-Gutierrez, Marta
Reinoso-Lozano, Francisco
Rodríguez-Revillas, Ana
Rodríguez Saenz de Urturi,
Alejandro
Romero-Imaz, Lucía
Sánchez-Rico, Susana
Sánchez-Santiuste, Mónica
Serrano de la Fuente, Patricia
Serrano-Martín, Henar
Silva-Freire, Thamires
Soria-Alcaide, Eva
Suárez-Plaza, Andrés Enrique
Tejero-Soriano, Beatriz
Torrecillas-Mainez, Andrea
Torres-Cortés Javier
Valentín-Pastrana Aguilar,
María de las Mercedes
Villanueva-Freije, Angélica
Virgós-Varela, Marta
Yagüe-Barrado, Marta
Yustas-Benitez, Natalia
Nuñez, María Concepción
Montserrat, Jaime
Queiruga, Javier
Rodriguez-Mariblanca, Amelia
Martínez de Soto, Lucía
Urroz, Mikel
Seco, Enrique
Zubimendi, Mónica
Stuart, Stephan
Díaz, Lucía
García, Irene
García Morales, María Teresa
Martín-Vega, Alberto
Caro, Abel
Martínez-Alés, Gonzalo