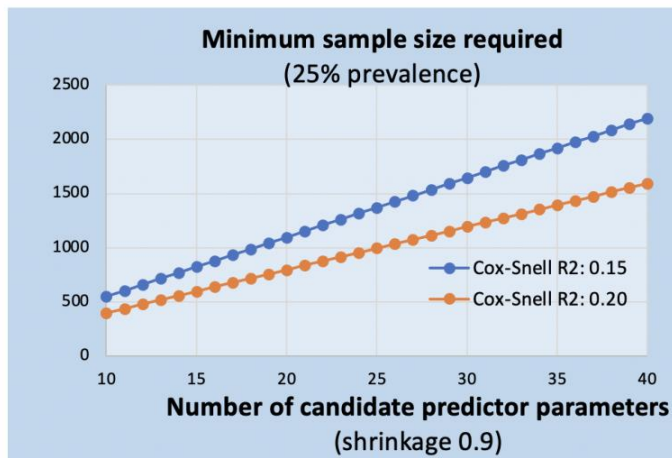


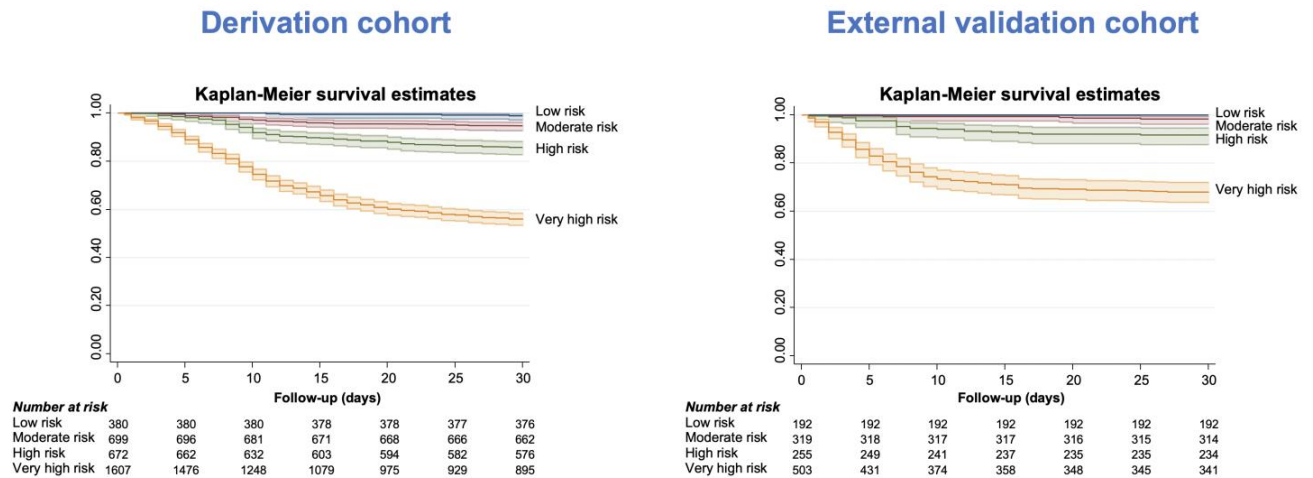
Appendix Figure 1. Sample size Calculation*

Parameters	Minimum sample size required (shrinkage of 0.9 and 25% prevalence)	
	Cox-Snell R ² : 0.15	Cox-Snell R ² : 0.20
10	549	398
15	823	597
20	1,097	796
25	1,372	995
30	1,646	1,194
35	1,920	1,393
40	2,194	1,592

To estimate a 30-parameter logistic model with a shrinkage of 0.9, a prevalence of events of 25% and assuming a Cox-Snell R² of 0.15, 1,646 individuals would be needed, approximately 14 events per variable. In our study, the estimated models were carried out with much higher sample size and 30 parameters were never exceeded, despite the categorization of some independent variables such as age.

*Riley RD, Ensor J, Snell KIE, Harrell FE, Jr., Martin GP, Reitsma JB, et al. Calculating the sample size required for developing a clinical prediction model. *BMJ*. 2020;368:m441. doi: 10.1136/bmj.m441.

Appendix Figure 2. Kaplan-Meier survival plots with 95% confidence intervals for the different 30-day mortality risk categories according to the simplified score in the derivation and validation cohorts.



We considered the risk of 30-day mortality as low with 0-2 points, moderate with 3-5, high with 6-8, and very high with 9-30.

Appendix Table 1. TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.
Introduction			
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.
Methods			
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.
	5b	D;V	Describe eligibility criteria for participants.
	5c	D;V	Give details of treatments received, if relevant.
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.
Predictors	7a	D;V	Clearly define all predictors used in developing the multivariable prediction model, including how and when they were measured.
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.
Sample size	8	D;V	Explain how the study size was arrived at.
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.
	10c	V	For validation, describe how the predictions were calculated.
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.
Risk groups	11	D;V	Provide details on how risk groups were created, if done.
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.
Results			

Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	Results. Participants epigraph.
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	Results. Participants epigraph. Table 1.
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	Results. Participants epigraph. Table 1.
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	Results. Model development and performance epigraph. Table 2.
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	Results. Model development epigraph. Table 3.
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	Results. Model development and Simplified score development epigraphs. Tables 3 and 5.
	15b	D	Explain how to use the prediction model.	Results. Model development and Simplified score development epigraphs. Table 5 and Figure 1.
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	Results. Model development and Simplified score development epigraphs. Appendix Table 2.
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	Non-applicable
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	Discussion. Paragraph n° 4.
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	Non-applicable.
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	Discussion. Paragraphs n° 1 - 3.
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	Discussion. Paragraphs n° 5.
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Methods section. Source of data epigraph. ClinicalTrials.gov (NCT04355871). European Union Electronic Register of Post-Authorization Studies (EUPAS34331). References section. References number 24 and 25
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	Title page and Abstract.

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

Appendix Table 2. Performance of the final prediction model and the simplified score.

	N° Participants	AUROC	95% CI
Primary analysis *			
Final prediction model			
Derivation cohort	3,358	0.822	0.806 – 0.837
External validation cohort	1,269	0.845	0.819 – 0.870
Simplified score			
Derivation cohort	3,358	0.806	0.790 – 0.821
External validation cohort	1,269	0.831	0.806 – 0.856
Sensitivity analysis 1 †			
Final prediction model			
Derivation cohort	4,031	0.822	0.809 – 0.836
External validation cohort	2,202	0.850	0.831 – 0.867
Simplified score			
Derivation cohort	4,031	0.805	0.791 – 0.820
External validation cohort	2,202	0.848	0.830 – 0.866
Sensitivity analysis 2 ‡			
Final prediction model			
Derivation cohort	4,031	0.818	0.805 – 0.832
External validation cohort	2,202	0.859	0.842 – 0.876
Simplified score			
Derivation cohort	4,031	0.806	0.791 – 0.820
External validation cohort	2,202	0.849	0.831 – 0.866

Abbreviations: AUROC; Area Under the Receiver Operating Characteristics; CI, confidence interval

* Primary analysis: Complete-case analysis without recoding missing values for predictors.

† Sensitivity analysis 1: Recoding missing values for predictors as a separate category.

‡ Sensitivity analysis 2: Missing values for predictors were given the value of the reference category for the variable.

Appendix Table 3. Simplified score to predict 30-day mortality in hospitalized patients with COVID-19 in the external validation cohort: Sensitivity, specificity, likelihood ratios, and predictive values for the different scores (0 to 30) in the validation cohort.

Score	Participants			Sen (%)	Spe (%)	+LR	1/-LR	PPV (%)	NPV (%)
	Total	Dying within 30-days							
		N ^o	%						
0	20	0	0.0	100	0.0	1	.	14.8	.
1	68	0	0.0	100	1.9	1.019	.	15.1	100
2	104	0	0.0	100	8.1	1.089	.	15.9	100
3	103	0	0.0	100	17.8	1.216	.	17.5	100
4	109	1	0.9	100	27.3	1.375	.	19.3	100
5	107	4	3.74	99.5	37.3	1.586	70.090	21.6	99.8
6	112	5	4.46	97.3	46.8	1.830	17.600	24.1	99.0
7	80	8	10.0	94.7	56.7	2.187	10.660	27.6	98.4
8	63	8	12.7	90.4	63.4	2.468	6.618	30.0	97.4
9	42	8	19.1	86.2	68.5	2.732	4.950	32.2	96.6
10	45	12	26.7	81.9	71.6	2.884	3.959	33.4	95.8
11	45	11	24.4	75.5	74.7	2.980	3.051	34.1	94.6
12	26	5	19.2	69.7	77.8	3.139	2.566	35.3	93.7
13	18	7	38.9	67.0	79.7	3.308	2.418	36.5	93.3
14	19	5	26.3	63.3	80.8	3.290	2.200	36.4	92.7
15	27	9	33.3	60.6	82.1	3.379	2.085	37.0	92.3
16	32	10	31.2	55.9	83.7	3.430	1.896	37.4	91.6
17	40	14	35.0	50.5	85.8	3.547	1.734	38.2	90.9
18	49	16	32.6	43.1	88.2	3.639	1.549	38.8	89.9
19	41	13	31.7	34.6	91.2	3.934	1.394	40.6	88.9
20	23	9	39.1	27.7	93.8	4.463	1.297	43.7	88.2
21	17	6	35.3	22.9	95.1	4.665	1.233	44.8	87.6
22	17	7	41.2	19.7	96.1	5.065	1.197	46.8	87.3
23	12	4	33.3	16.0	97.0	5.391	1.155	48.4	86.9
24	15	8	53.3	13.8	97.8	6.229	1.135	52.0	86.7
25	13	5	38.5	9.6	98.4	6.088	1.088	51.4	86.2
26	9	4	44.4	6.9	99.2	8.306	1.065	59.1	86.0
27	8	6	75.0	4.8	99.6	12.940	1.046	69.2	85.7
28	3	1	33.3	1.6	99.8	8.625	1.014	60.0	85.4
29	2	2	100	1.1	100	-	1.011	100	85.3
30	0	-	-	-	-	-	-	-	-

Abbreviations: Sen, sensitivity; Spe, specificity; +LR, positive likelihood ratio; -LR, negative likelihood ratio; PPV, positive predictive value; NPV, negative predictive value.

Appendix Table 4. The COVID-19@Spain Study Group.

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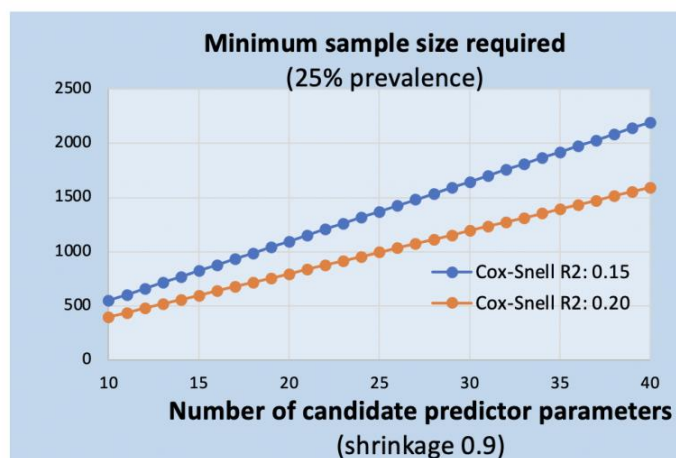
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Appendix Figure 1. Sample size Calculation*

Parameters	Minimum sample size required (shrinkage of 0.9 and 25% prevalence)	
	Cox-Snell R ² : 0.15	Cox-Snell R ² : 0.20
10	549	398
15	823	597
20	1,097	796
25	1,372	995
30	1,646	1,194
35	1,920	1,393
40	2,194	1,592

To estimate a 30-parameter logistic model with a shrinkage of 0.9, a prevalence of events of 25% and assuming a Cox-Snell R² of 0.15, 1,646 individuals would be needed, approximately 14 events per variable. In our study, the estimated models were carried out with much higher sample size and 30 parameters were never exceeded, despite the categorization of some independent variables such as age.

*Riley RD, Ensor J, Snell KIE, Harrell FE, Jr., Martin GP, Reitsma JB, et al. Calculating the sample size required for developing a clinical prediction model. *BMJ*. 2020;368:m441. Epub 2020/03/20. doi: 10.1136/bmj.m441. PubMed PMID: 32188600.